Webappendix for: Responding to growing global stimulant use: challenges and opportunities

Contents

Summary of overall approach to reviewing literature for this paper

This section summarises the broad approach used in searching for evidence during the writing of this paper.

- We systematically searched for high-quality reviews that involved quantitative synthesis where appropriate, in preference to other kinds of reviews. Details of the search strategies used for each component of the paper are summarised in this appendix.
- If no such review could be located, we selected narrative reviews if they clearly described the search strategy and inclusion/exclusion criteria for their review.
- If no such reviews could be located, we conducted searches for high quality single studies with the highest possible quality level for the issue being examined (e.g. well-conducted randomised controlled trials if searching for evidence on an intervention's efficacy).
- If no such studies could be located, we included lower-quality evidence but noted this clearly in tables and text.
- For some key areas, e.g. overdose, only older reviews could be located ([1,2]), so we conducted new full systematic reviews to up date and expand upon previous reviews.
- For the mathematical modelling component for each parameter we conducted systematic searches along the same logic to obtain the most robust estimated parameters.

Webappendix A: Types of stimulants that may be used extra-medically

Cocaine: A natural product extracted from coca leaves (Erthroxylon coca Lam leaves) and can be produced as either a hydrochloride salt or free base. Cocaine base and hydrochloride salt both appear as white powders while crack cocaine usually appears as small 'rocks'. The effects of cocaine are very similar to those of amphetamine: both increase activity of the noradrenergic and dopaminergic synapses. When taken illicitly, cocaine is normally snorted or smoked if in crack form. Less common it is injected or ingested.

Amphetamine: A synthetic substance, from the phenethylamine family (*N*,α-methylphenethylamine), is normally found in powder form. It can also be found in tablets with similar logos to ecstasy or MDMA tablets. Amphetamine is a central nervous system stimulant that increases noradrenaline and dopamine neurotransmitter activity, causing hypertension and tachycardia. Acute effects include increased confidence, sociability and energy as well as suppressed hunger and fatigue. Users can later experience irritability, restless, anxiety, depression, lethargy and insomnia. Amphetamine can be ingested, snorted and less commonly injected.

Methamphetamine: A synthetic substance similar to amphetamine also in the phenethylamine family (*N*,α-dimethylphenethylamine). Methamphetamine is more potent than amphetamine and found as powder, within tablets with similar logos to ecstasy or MDMA tablets, or in crystalline 'ice' form. The effects of amphetamine and methamphetamine are the same so the increased potency of methamphetamine can be difficult for users to distinguish. Methamphetamine can be used in the same forms as amphetamine with 'ice' able to be smoked.

MDMA: A synthetic substance abbreviated from methylenedioxy-methylamphetamine, and commonly known as ecstasy. It is commonly found in tablet or pill form with a characteristic logo but can also be found as powders or capsules. As MDMA is a ring-substituted phenethylamine, its effects slightly differ from the amphetamines and other stimulants: euphoria, increased sensory awareness and mild CNS stimulation. In tablet form, MDMA is primarily ingested but it can be snorted, inhaled or injected in powder form.

Ephedrine: A stimulant similar to amphetamine used medicinally to treat low blood pressure, asthma, narcolepsy and obesity. Ephedrine is commonly either ingested or injected because it is water soluble. It can be used to produce methamphetamine illicitly.

Benzedrine: Brand name of the first pharmaceutical amphetamine, originally marketed as a decongestant inhaler that was widely used extra-medically. It can produce euphoria and stimulation (**see also Panel C - Populations of interest).**

Adrenalin: Adrenalin acts on the adrenergic receptors to stimulate the CNS. It has medicinal uses for anaphylaxis, cardiac arrest and overdose and can be administrated by injection or inhalation.

BZP and other piperazine derivatives: A synthetic substance, despite natural product claims, commonly found in tablets or capsules and loose powders. BZP (*N*-benzylpiperazine) is a CNS stimulant with a reduced potency than dextroamphetamine. It produces amphetamine-like effects such as increased heart rate, blood pressure and pupil dilation. Other piperazine derivatives produce similar effects to MDMA. These drugs are mostly found in tablet form and ingested with the powder rarely injected or snorted.

Khat Khat is a herbal product consisting of the leaves and shoots of the shrub *Catha edulis*. Fresh leaves of khat contain the stimulants cathinone and cathine, both of which increase the release of dopamine from CNS dopamine terminals. Khat's natural range extends throughout East Africa from Ethiopia, Eritrea and Somalia, through to South Africa; it is also found in Rwanda, Zaire, Malawi and Zimbabwe. In the past khat use was geographically limited because it loses its efficacy after a few days. However, the migration of khat-using communities to other continents has spread its use over the last two decades to Western Europe, North America and Australia.[3]

Cathinone derivatives (e.g. flephedrone, mephredrone): A group of synthetic substances related to the p cathinone and the phenethylamine family. They are normally found as powders (white, brown, or crystalline) but can also be found in capsules. Cathinone derivatives are commonly snorted, ingested or injected because water soluble. These drugs behave like less potent CNS stimulants producing similar effects to amphetamines, cocaine and MDMA.

Webappendix B: Medicinal uses of stimulants

Stimulants have a long history of medicinal use. Cocaine was used widely as a local anaesthetic through the 19th century, particularly in eye surgery, however, it has been largely replaced by structurally similar compounds (e.g., procaine) that have similar efficacy[4] but lower risk of toxicity[5] and dependence liability.[4,6,7] Amphetamines were promoted for their decongestant and antidepressant properties, and also used for weight loss,[8] through the 20th century.[9,10] Because of the potential for abuse and adverse reactions (insomnia, dehydration, nervousness, psychosis and pulmonary hypertension)[11] less potent psychostimulants, such as phentermine and methylphenidate, have largely replaced the use of amphetamine and methamphetamine in medicine.[12] Despite this, the global prescription-based consumption of amphetamine has risen over the past two decades,[13] with ADHD in children being the most common indication for prescription.

Attention Deficit Hyperactivity Disorder (ADHD): ADHD is a childhood onset psychiatric disorder characterised by inattention, impulsivity, and hyperactivity, which can persist into adulthood. Recent Cochrane reviews have found that, across varied age groups, amphetamines improve the core symptoms of ADHD within short-term treatments with no significant difference between the different classes and formulations of amphetamines.[14,15] Only mixed amphetamine salts compound improved retention in ADHD treatment in adults.[14] However, higher quality studies investigating the effect of amphetamines, both in the short and long-term use, on ADHD symptoms are needed. Rates of ADHD are elevated amongst people who have a primary substance use disorders (estimated at 23%[16]). However there is currently no substantive evidence that the prescription of stimulants for ADHD increases the risk of subsequent illicit stimulant use or developing a substance use disorders.[17-21]

Weight loss: Few medications are now used for weight loss and those that are available are best reserved for individuals with high BMI's. Amphetamines were used as appetite suppressants to treat obesity in the 1930s.[8] However, this use of amphetamines has been discontinued except for short-term use because of the potential risks.[11] Psychostimulants that activate the catecholamine pathway such as phentermine, have largely replaced the amphetamines. Anorectic drugs which promote serotonin neurotransmission don't have stimulant or sympathomimetic properties and are an alternative as are medications that block lipase activity.

Local anaesthetic: Cocaine solution, administered either as a nasal spray or cream, has been widely used as a local anaesthetic by ear, nose and throat surgeons because it also has a decongestant effect that facilitate instrumental access to the nasal cavity.[22] Cocaine reduces sodium ion permeability and increases the action potential threshold. It also interferes norepinephrine reuptake, resulting in the vasoconstriction. A recent Cochrane review found that there were no serious side-effects following use of cocaine-containing topical anaesthetics.[4] However, there are now a variety of alternative medication formulations that also provide topical anaesthesia.

Webappendix C: Details of UNODC process for collation and reporting of data on amphetamine and cocaine seizures and importation routes

A description of the overall approach to collation and reporting adapted from the UNODC's 2018 World Drug Report[23] is below:

The analysis presented in this report is mainly derived from the ARQ responses from Member States up to the 2016 reporting year. Including information from other sources, UNODC was able to obtain seizure data from 128 countries and territories for 2016. Over the 2011-2016 period seizures from in total 161 countries and territories were obtained. Seizures are thus the most comprehensive indicator of the drug situation and its evolution at the global level. Although seizures may not always reflect trafficking trends correctly at the national level, they tend to show reasonable representations of trends at the regional and global levels.

Seizures are reported in volume terms as well as in terms of the number of seizure cases. The analysis of seizure cases enables a direct comparison of data across drug categories. Reporting of seizure cases is, however, less comprehensive. A total of 69 countries and territories reported seizure cases to UNODC in 2016, or 103 countries and territories over the 2011-2016 period.

Countries reporting seizures of drug in volume terms may report seizures using a variety of units, primarily by weight (kg) but also in litres, tablets, doses, blotters, capsules, ampoules, et cetera. When reporting about individual countries in individual years, UNODC endeavours to be as faithful as possible to the reports received, but often it is necessary to aggregate data of different types for the purposes of comparison. For the aggregation, conversion factors are used to convert the quantities into 'kilogram equivalents' (or 'ton equivalents').

Webappendix D: Details of UNODC data on amphetamine and cocaine use

Data on the annual prevalence of amphetamine and cocaine use as a percentage of the population age 15-64 were obtained from the UNODC World Drug Report 2018, available from https://www.unodc.org/wdr2018/. Data from individual countries are mainly sourced from UNODC's Annual Report Questionnaire (ARQ), which collects and reports data on extent, patterns and trends in drug use and its health consequences across the world. The World Drug Report also incorporates data from the literature and grey literature, such as from government sources, academic research, and major international surveys that monitor drug use.

Estimates of the prevalence of cocaine and amphetamine use are computed using various adjustments, and imputation for countries where data are missing based on countries in the same subregion. Upper and lower uncertainty range estimates are calculated at a 90% confidence interval among those aged 15-64 years.

Table C1: Regional estimates of past year use of stimulants reported in UNODC's World Drug Report 2018

Region or subregion	Cocaine[a]						Amphetamines[b] and prescription stimulants						"Ecstasy"					
	Number (thousands)			Prevalence (percentage)			Number (thousands)			Prevalence (percentage)			Number (thousands)			Prevalence (percentage)		
	Best estimate	Lower	Upper	Best estimate	Lower	Upper	Best estimate	Lower	Upper	Best estimate	Lower	Upper	Best estimate	Lower	Upper	Best estimate	Lower	Upper
Africa	**3,180**	**920**	**5,720**	**0.47**	**0.13**	**0.84**	**5,980**	**1,910**	**10,420**	**0.88**	**0.28**	**1.53**	**1,410**	**450**	**2,420**	**0.21**	**0.07**	**0.36**
East Africa	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
North Africa	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Southern Africa	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
West and Central Africa	1,805	725	2,890	0.69	0.28	1.11	-	-	-	-	-	-	-	-	-	-	-	-
Americas	**9,230**	**8,510**	**9,880**	**1.39**	**1.28**	**1.49**	**7,530**	**6,210**	**8,790**	**1.13**	**0.93**	**1.32**	**3,480**	**3,370**	**3,610**	**0.52**	**0.51**	**0.54**
Caribbean	180	80	330	0.63	0.29	1.16	260	10	710	0.90	0.05	2.48	60	30	100	0.23	0.10	0.36
Central America	200	100	300	0.66	0.35	1.01	60	30	90	0.21	0.09	0.31	50	20	100	0.17	0.07	0.33
North America	6,140	5,990	6,280	1.91	1.86	1.95	6,500	5,540	7,240	2.02	1.72	2.25	2,860	2,860	2,860	0.89	0.89	0.89
South America	2,720	2,340	2,970	0.95	0.82	1.04	710	630	740	0.25	0.22	0.26	510	470	550	0.18	0.16	0.19
Asia	**1,040**	**150**	**1,940**	**0.03**	**0.01**	**0.07**	**17,450**	**2,690**	**32,220**	**0.59**	**0.09**	**1.08**	**11,200**	**1,270**	**21,140**	**0.38**	**0.04**	**0.71**
Central Asia	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
East and South-East Asia	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Near and Middle East	70	30	130	0.02	0.01	0.04	-	-	-	-	-	-	-	-	-	-	-	-
South Asia	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Europe	**4,330**	**3,870**	**4,880**	**0.79**	**0.71**	**0.90**	**2,850**	**2,290**	**3,450**	**0.52**	**0.42**	**0.63**	**4,050**	**3,490**	**4,740**	**0.74**	**0.64**	**0.87**
Eastern and South-Eastern Europe	620	290	1,000	0.28	0.13	0.44	720	400	1,060	0.32	0.18	0.47	1,330	840	1,840	0.59	0.37	0.82
Western and Central Europe	3,710	3,580	3,890	1.16	1.12	1.22	2,130	1,900	2,390	0.67	0.59	0.75	2,720	2,650	2,900	0.85	0.83	0.91
Oceania	**430**	**420**	**430**	**1.65**	**1.61**	**1.65**	**350**	**320**	**360**	**1.34**	**1.24**	**1.38**	**420**	**400**	**420**	**1.64**	**1.56**	**1.65**
Australia and New Zealand	420	420	420	2.19	2.19	2.19	250	250	250	1.34	1.34	1.34	410	400	420	2.17	2.12	2.23
Melanesia	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Micronesia	-	-	-	-	-	-	6	2	11	1.63	0.58	3.15	-	-	-	-	-	-
Polynesia	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
GLOBAL ESTIMATE	**18,200**	**13,870**	**22,850**	**0.37**	**0.28**	**0.47**	**34,160**	**13,420**	**55,240**	**0.70**	**0.27**	**1.13**	**20,570**	**8,990**	**32,340**	**0.42**	**0.18**	**0.66**

Webappendix E: Groups which may have higher levels of stimulant use

Men who have sex with men (MSM)

Stimulants are often used to increase sexual desire, make intercourse more pleasurable, decrease sexual inhibition, facilitate sexual experimentation, and make anal intercourse easier and less painful. Stimulants are often taken with oral erectile dysfunction medications to enhance sexual performance and facilitate 'sexual marathons', often referred to as 'chem sex'. These attributes in sexually adventurous gay subcultures facilitate risky sexual behaviours, including unprotected sex, forceful and prolonged sexual contact (increasing the likelihood of condom failure) and lesions caused by forceful sexual penetration, all of which increase the risk of HIV, HCV and STI transmission.[24] Over the past decade, stimulant use has become increasingly popular among MSM in North America, Asia, Western and South Western Europe The 12-month prevalence of stimulant use among MSM in high income countries (North America and UK) has been reported to range from 7.2-18.8%. Growing evidence links stimulant use among MSM with unprotected anal intercourse, and systematic reviews demonstrate an increased odds of HIV infection among MSM who used meth/amphetamines (odds ratio 2.73, 95%CI: 2.16 to 3.46).[24] HIV, HCV and STI prevention programs targeting MSM should take into account the role of ATS in disease transmission.

Occupational Exposure

Truck drivers who operate long-haul and often night-time routes use stimulants to maintain alertness. In Brazil for example, a random roadside test of 500 truck drivers found that 9% tested positive for drugs, with the majority (62%) amphetamines.[25] Drivers predominantly used fenproporex and diethylpropion to stay awake. Use of amphetamines by truck drivers increases risks of motor vehicle accidents and transport injuries, in addition to the health-related harms outlined in **Table 2**.

Armed forces

Stimulants were used by the military environment in the second world war. As the nature of warfare has shifted to long, nocturnal missions and round-the-clock (continuous) operations, there has been increased interest to use stimulants to improve alertness and energy. Dexedrine (referred to as "go-pills") was prescribed to pilots during the Gulf war.

People in manual labour occupations

There have been substantial increases arrests for methamphetamine use in north-east Thailand, a region where a large proportion of people work on rubber plantations. Locals report using "ya ba" or "ya ma" (methamphetamine in pills mixed with caffeine) to increase energy and alertness – allowing them to work multiple jobs and "tap" rubber trees in the cool hours of the very early morning.[26] Use of methamphetamine (referred to locally as "shabu") has also been reported among Filipino immigrants working in the hospitality sector to work long work and maintain multiple jobs. In many instances, the drug is used solely for occupational reasons rather than recreationally, thereby reducing the perceived need for treatment.

Sex Workers

Sex workers, particularly street-based or freelance ones rather than entertainment and brothel-based report high rates of stimulant use and risky sexual practices, increasing their risks of HIV, HCV and STI infection. A prospective cohort of young sex workers in Phnom Penh found that 26% reported recent "ya ma" use that was associated with sexually transmitted infections.[27] Sex workers who use stimulants often reported more sex partners and higher levels of other substance use, increasing the risk of negative health effects.

Webappendix F: Details of Global Burden of Disease 2017 study data for amphetamine and cocaine dependence

Burden was quantified by geography, for 20 age groups covering 0-99 years, both sexes, and timepoints spanning the period 1990 to 2017. Comprehensive methods for estimating YLDs, YLLs, and DALYs have been presented in a series of publications[28-31]

YLLs

Input data on causes of death data came from vital registration, verbal autopsy and surveillance databases dating back to 1980.[28,31] Normative life tables were generated using data on the lowest death rates for each age group within geographies with total populations of more than 5 million. YLLs were then estimated by multiplying cause-specific deaths at a given age by the standard life expectancy at that age obtained from this normative life table. Full details of all the modelling process have been published previously.[28,31]

The Cause of Death Ensemble modelling (CODEm) strategy was used to model cause of death data by location, age, sex, and year for opioids.[28,31] CODEm model outputs for all GBD causes were then rescaled to fit the all-cause mortality envelope to derive final cause-specific deaths; deaths coded as alcohol and drug poisonings were attributed to the relevant alcohol and drug use disorders.

YLDs

Epidemiological disease models

Systematic reviews of the literature were conducted to compile data on the prevalence, incidence, remission, and excess mortality associated with opioid dependence. Electronic databases (PubMed, EMBASE, PsycINFO) and grey literature sources were searched in accordance with the Preferred Reporting Items for Systematic Reviews (PRISMA) guidelines.[32] For each epidemiological parameter, eligible estimates were derived from studies published since 1980.

The epidemiological data obtained from systematic literature reviews were modelled in DisMod-MR 2.1. This is a Bayesian meta-regression tool which pools data-points from different sources and adjusts for known sources of variability (e.g. differences in case definitions and sampling method) to produce internally consistent estimates of incidence, prevalence, remission, and excess mortality.[33] It is also used to estimate the epidemiology of disorders within areas with limited data. DisMod-MR 2.1 analyses ran in a sequence of estimations at each level of the GBD geographic hierarchy (global, super-region, region, country, and if applicable, subnational locations) with consistency imposed between estimates at each level. More information on DisMod-MR 2.1 has been presented in other publications.[28-31]

Although our inclusion criteria ensured minimum study quality, there was considerable variability between studies that reflected different methodologies and analyses (e.g. see[34-38]). Uncertainty in both the

epidemiological data and in modelling was propagated to the final prevalence output used to calculate YLDs. This was in addition to the uncertainty from fixed effects and random effects for country and regions.[33]

Disability weights

Each country, age, sex, and year-specific prevalence derived by DisMod MR 2.1 was multiplied by a disorder-specific disability weight to estimate YLDs. Disability weights ranged from 0 ('perfect health') to 1 ('death') to quantify the severity of the health loss associated with a given disease or injury. They were obtained from population surveys in a number of different countries and from an open-access survey available in multiple languages in which lay participants were presented with pairs of short descriptions of health states and asked to rate which they considered the more 'unhealthy'.[39-41] Disability weights were generated for all sequelae of diseases and injuries. Further details regarding disability weight methodology has been published previously[40-42].

Disability-adjusted life-years (DALYs)

The burden calculation involved (1) aggregating substance use disorder-specific epidemiological data and disability weights to calculate prevalent YLDs[30]; (2) multiplying substance use disorder-specific estimates of mortality by standard life expectancy at the age of death to calculate YLLs[43,44]; and (3) summing YLDs and YLLs to generate substance use disorder-specific DALYs[45].

DALYs were derived by summing YLD and YLLs for each disorder, location, age group, sex, and year. Age-standardised rates of prevalence, deaths, YLLs, YLDs, and DALYs were estimated using the GBD world population age standard. Uncertainty was derived for all estimates by simulating 1000 draws from each estimate's posterior distribution. This captures uncertainty arising from primary inputs, sample sizes in the data collected, adjustments made to the data during modelling, and model estimation. For YLLs, they capture uncertainty due to study sample sizes, adjustments made to the all-cause mortality data, and model estimation.

Table F1: Prevalence of amphetamine and cocaine dependence and mortality due to amphetamines and cocaine, Global Burden of Disease 2017

	Amphetamines				Cocaine			
	Dependence cases ('000s) (95%UI)	Age-standardised rate per 100,000 (95%UI)	Number of deaths (in 1000's)	Death rates (per 100,000)	Dependence cases ('000s) (95%UI)	Age-standardised rate per 100,000 (95%UI)	Number of deaths (in 1000's)	Death rates (per 100,000)
Andean Latin America	51.6 (35.1-72.7)	77.2 (66.4-90.5)	<0.1 (<0.1-<0.1)	<0.1 (<0.1-0.1)	48.6 (41.7-56.9)	79.4 (54.3-111.4)	<0.1 (<0.1-<0.1)	<0.1 (<0.1-<0.1)
Australasia	160.0 (138.1-179.3)	623.7 (537.0-702.4)	<0.1 (<0.1-0.1)	0.2 (0.1-0.2)	38.6 (33.6-44.3)	140.6 (121.1-163.1)	<0.1 (<0.1-<0.1)	<0.1 (<0.1-<0.1)
Caribbean	13.7 (10.5-17.5)	28.6 (21.9-36.6)	<0.1 (<0.1-<0.1)	<0.1 (<0.1-<0.1)	33.0 (28.6-38.2)	68.5 (59.3-79.5)	<0.1 (<0.1-<0.1)	0.1 (<0.1-0.1)
Central Asia	83.3 (60.2-113.5)	84.9 (61.3-115.2)	<0.1 (<0.1-<0.1)	<0.1 (<0.1-0.1)	24.3 (20.6-28.6)	25.5 (21.7-30.0)	0.1 (0.1-0.1)	0.1 (0.1-0.1)
Central Europe	120.5 (95.3-151.2)	126.3 (97.5-162.5)	<0.1 (<0.1-<0.1)	<0.1 (<0.1-<0.1)	66.5 (58.3-76.0)	57.7 (49.5-67.0)	<0.1 (<0.1-<0.1)	<0.1 (<0.1-<0.1)
Central Latin America	267.2 (180.5-386.4)	97.8 (66.5-140.9)	0.1 (<0.1-0.1)	<0.1 (<0.1-<0.1)	424.8 (372.7-487.3)	159.5 (140.1-182.7)	0.1 (0.1-0.1)	<0.1 (<0.1-0.1)
Central Sub-Saharan Africa	30.7 (22.8-40.9)	26.0 (19.6-34.2)	<0.1 (<0.1-0.1)	<0.1 (<0.1-0.1)	6.8 (5.5-8.4)	7.2 (5.9-8.6)	0.1 (<0.1-0.1)	0.1 (<0.1-0.1)
East Asia	2424.6 (1683.3-3369.3)	180.8 (122.8-255.8)	0.6 (0.4-0.7)	<0.1 (<0.1-<0.1)	109.1 (89.6-133.3)	6.4 (5.2-7.9)	0.3 (0.2-0.4)	<0.1 (<0.1-<0.1)
Eastern Europe	249.0 (186.7 -325.3)	134.0 (97.5-178.7)	0.4 (0.3-0.4)	0.2 (0.1-0.2)	166.8 (147.7-188.9)	80.6 (70.7-91.7)	0.8 (0.7-0.8)	0.3 (0.3-0.3)
Eastern Sub-Saharan Africa	92.2 (68.3-122.6)	24.0 (18.2-31.3)	0.1 (<0.1-0.2)	<0.1 (<0.1-0.1)	11.4 (8.8-14.6)	3.8 (3.0-4.7)	0.1 (<0.1-0.2)	<0.1 (<0.1-0.1)
High-income Asia Pacific	128.5 (96.3-167.3)	85.7 (62.4-114.3)	<0.1 (<0.1-<0.1)	<0.1 (<0.1-<0.1)	182.7 (161.9-206.1)	102.0 (88.6-116.6)	<0.1 (<0.1-<0.1)	<0.1 (<0.1-<0.1)
High-income North America	969.7 (712.5-1271.4)	296.9 (214.9-393.5)	2.0 (0.6-2.4)	0.5 (0.2-0.6)	1937.8 (1752.2-2147.3)	539.2 (485.8-602.0)	4.4 (3.9-5.0)	1.0 (0.9-0.2)
North Africa and Middle East	231.6 (170.8 -302.3)	35.8 (26.4-46.6)	0.1 (0.1-0.2)	<0.1 (<0.1-<0.1)	220.7 (189.6-255.8)	35.9 (31.1-41.4)	0.2 (0.2-0.4)	<0.1 (<0.1-0.1)
Oceania	19.3 (12.8-28.0)	137.1 (92.2-197.4)	<0.1 (<0.1-<0.1)	<0.1 (<0.1-<0.1)	0.5 (0.4-0.7)	4.2 (3.3-5.4)	<0.1 (<0.1-<0.1)	<0.1 (<0.1-<0.1)
South Asia	122.7 (90.8-161.2)	6.7 (5.0-8.7)	0.4 (0.2-0.8)	<0.1 (<0.1-0.1)	90.7 (72.9-111.6)	5.1 (4.2-6.3)	0.4 (0.2-0.7)	<0.1 (<0.1-<0.1)
Southeast Asia	1549.4 (1020.6-2237.2)	225.0 (147.9-326.0)	0.1 (0.1-0.1)	<0.1 (<0.1-<0.1)	33.4 (26.6-41.4)	4.8 (3.8-5.9)	<0.1 (<0.1-<0.1)	<0.1 (<0.1-<0.1)
Southern Latin America	46.0 (32.3-64.0)	70.2 (48.9-97.4)	<0.1 (<0.1-<0.1)	<0.1 (<0.1-<0.1)	216.7 (193.1-246.1)	319.5 (284.6-363.2)	0.1 (<0.1-0.1)	0.1 (0.1-0.1)
Southern Sub-Saharan Africa	37.8 (28.6-50.0)	44.0 (33.5-57.8)	<0.1 (<0.1-<0.1)	<0.1 (<0.1-<0.1)	38.4 (33.2-44.5)	50.4 (44.1-57.9)	0.1 (<0.1-0.1)	0.1 (<0.1-0.1)
Tropical Latin America	223.4 (152.5-319.7)	98.9 (66.7-141.9)	<0.1 (<0.1-<0.1)	<0.1 (<0.1-<0.1)	654.3 (577.5-747.9)	278.6 (245.6-318.0)	0.2 (0.2-0.3)	0.1 (0.1-0.1)
Western Europe	466.3 (353.5-605.2)	135.8 (99.8-180.3)	0.3 (0.2-0.3)	0.1 (0.1-0.1)	690.3 (626.8-770.5)	170.1 (153.0-191.6)	0.1 (0.1-0.1)	<0.1 (<0.1-<0.1)
Western Sub-Saharan Africa	95.1 (70.0-126.3)	23.2 (17.4-30.0)	0.1 (0.1-0.1)	<0.1 (<0.1-0.1)	21.8 (18.0-26.3)	7.6 (6.4-8.8)	0.2 (0.1-0.3)	0.1 (0.1-0.2)
Global	**7382.6 (5376.5-9821.8)**	**95.9 (70.0-128.4)**	**4.5 (3.3-5.0)**	**0.1 (<0.1-0.1)**	**5017.2 (4521.0-5610.4)**	**63.7 (57.3-71.3)**	**7.3 (6.6-8.1)**	**0.1 (0.1-0.1)**

Webappendix G: Details of literature search on mortality among people who use amphetamine and cocaine

Description of methods

We utilised previously published reviews[46,47] to identify relevant studies published from 1980 to 2007 (amphetamine) and to 2008 (cocaine).

The Medline, Embase and PsycINFO peer-reviewed literature databases were searched using the OVID™ interface/platform for relevant articles published from 2008 to 22 February 2018 (amphetamine-type stimulants), and 2009 to 22 February 2018 (cocaine). Articles of interest comprised those likely to contain data describing all-cause and cause-specific crude mortality rates (CMR) and/or standardised mortality ratios (SMR) among people who used cocaine or amphetamine-type stimulants. Sets of search strings incorporating both keywords and Medical Subject Headings (MeSH terms) reflecting drug type and mortality epidemiology from the previous reviews were revised and expanded for this updated search. Searches were limited to human literature. No other restrictions were applied to the search; citations for papers in languages other than English were included and read via Google Translate. Citations from these searches were imported into an Endnote™ library, and duplicate citations removed.

To check for missing peer-review literature, reference lists for relevant systematic reviews identified in the peer-review literature search were hand searched for additional papers not already identified. A final list of included studies was distributed to experts to check if any relevant studies were missed.

Each set of search results (title and abstract) were first be screened by one team member in Covidence. All papers marked as excluded were reviewed by a second person to ensure accuracy in first-pass screening. Each study for full-text screening was reviewed in full by two people. Conflicts were resolved through discussion and referral to a third party if needed.

Data were independently extracted into an Excel worksheet template by one member of the research team and checked by a second member of the team, with data extraction discrepancies or errors checked and resolved by a third independent member of the team not involved in original data extraction. Bibliographic information was extracted in addition to study specific information. Data entry was standardized by use of a manual containing data entry rules. Where data were incomplete, authors were contacted via email to obtain additional information.

Variables extracted included study information and sample information (treatment status, HIV status, sex, percentage of sample injecting, treatment engagement). Crude mortality rates (CMRs) and standardized mortality ratios (SMRs) were extracted as mortality measures. Cause of death information (where reported) was extracted for AIDS, overdose, suicide, traumatic (accident, homicide, injury, violence and poisoning), disease-related deaths, and other key categories. Disease-related deaths were recoded according to the following categories; cardiovascular (endocarditis, myocardial infarction, circulatory system disease and cardiovascular disease), cerebrovascular, respiratory (pneumonia and chronic respiratory disease), liver (cirrhosis, viral hepatitis and liver disease), cancer (neoplasm, tumour and carcinoma), digestive (digestive system disease, nephritis and haemorrhage from duodenal ulcer), nervous system disease and other diseases (tuberculosis, bacterial infection, unspecified 'other disease' or 'natural causes' and when disease categories were not separated).

The quality index used in the previous reviews[46,47] was adopted for consistency. The quality index assesses each study on nine individual criteria: case ascertainment, measurement, diagnosis, estimate, numerator and denominator, data catchment, completeness, representativeness and age/sex variables. Each criterion will include a rating scale and the individual scores tallied to provide an overall quality score. Study information necessary for quality assessment will be extracted to the Excel template. The greater the quality score, the higher the methodological quality of the study.

Crude mortality rates were calculated as per 100 person-years. Where person-years were not reported nor made available by the authors, an approximate person-year of follow-up was calculated, with the assumption that deaths occurred halfway through the follow-up period, so that each case contributes half the person-year follow-up of survivors.

Estimates were analysed in subgroups according to population type (for example, estimates from cohorts recruited on the basis of having a chronic physical health condition associated with a high mortality rate may be considered separately). Random-effects meta-analyses to determine pooled all-cause and cause-specific CMR and SMR estimates were performed using STATA 15.0. This approach uses inverse variance weighting to calculate: fixed- and random effects pooled summary estimates; confidence limits; a test for differences between study effects; and an estimate of between-study variance. The random effects model allows for heterogeneity between as well as within studies; expecting high levels of heterogeneity between cohorts, the random-effects model was used in all meta-analyses, with confirmation through the heterogeneity c2 and I-squared statistic. To investigate the source of this heterogeneity in an attempt to reduce it, cohorts were divided into subsamples (e.g., by sex, age group, treatment status and HIV status) and/or these factors studied as possible risk factors for mortality via meta-regression in Stata.

Search strings for electronic literature searches

Search date: 22 February 2018.

Database	Search group	Search terms
Medline*	ATS	ATS or amphet* or meth?amphet* or deoxyephedrine or desoxy* or madrine or metamfet* or methylamphet* or n?methylamphet* or d?amphet* or dextro?amphet* or dexamphet* or dexedrine or stimulant* or ecstasy or MDMA or lisdexamfetamine or methylphenidate or modafinil **exp Amphetamine/ or exp Amphetamines/ or exp Dextroamphetamine or exp P-Chloroamphetamine/ or exp 2,5-Dimethoxy-4-Methylamphetamine/ or exp P-hydroxyamphetamine/ or exp Iofetamine/ or exp Methamphetamine/ or exp Benzphetamine/ or exp Phentermine/ or exp Chlorphentermine/ or exp Mephentermine/ or exp Amphetamine-Related Disorders/ or exp N-Methyl-3,4-Methylenedioxyamphetamine/ or exp Lisdexamfetamine Dimesylate/ or exp Methylphenidate/**

Database	Search group	Search terms
	Cocaine	Cocaine **exp Cocaine/ or exp Crack Cocaine/ or exp Cocaine-Related Disorders/ or exp Cocaine Smoking/**
	Mortality	Mortal* or fatal* or death* **exp DEATH/ or exp "CAUSE OF DEATH"/ or exp DEATH, SUDDEN/ or exp Fatal Outcome/ or exp Mortality/**
EMBASE#	ATS	ATS or amphet* or meth?amphet* or deoxyephedrine or desoxy* or madrine or metamfet* or methylamphet* or n?methylamphet* or d?amphet* or dextro?amphet* or dexamphet* or dexedrine or stimulant* or ecstasy or MDMA or lisdexamfetamine or methylphenidate or modafinil **exp Amphetamine/ or exp Amphetamine Derivative/ or exp Methamphetamine/ or exp Dexamphetamine/ or exp Iofetamine I 125/ or exp Iofetamine I 123/ or exp Iofetamine/ or exp 4 Methoxyamphetamine/ or exp Hydroxyamphetamine or exp Mephentermine/ or exp Phentermine/ or exp Benzphetamine/ or exp Chloramphetamine/ or exp Chlorphentermine/ or exp Midomafetamine/ or exp Methylphenidate/ or exp Lisdexamfetamine/ or exp Modafinil/**
	Cocaine	Cocaine **exp Cocaine/ or exp Cocaine Dependence/ or exp Cocaine Derivative/**
	Mortality	Mortal* or fatal* or death* **exp DEATH/ or exp "CAUSE OF DEATH"/ or exp ACCIDENTAL DEATH/ or exp SUDDEN DEATH/ or exp Fatality/ or exp Mortality/**
PsychINFO^	ATS	ATS or amphet* or meth?amphet* or deoxyephedrine or desoxy* or madrine or metamfet* or methylamphet* or n?methylamphet* or d?amphet* or dextro?amphet* or dexamphet* or dexedrine or stimulant* or ecstasy or MDMA or lisdexamfetamine or methylphenidate or modafinil **exp Dexamphetamine/ or exp Methamphetamine/ or exp Amphetamine/ or exp Methylenedioxymethamphetamine/ or exp Methylphenidate/ or exp Dextroamphetamine/**
	Cocaine	Cocaine **exp Cocaine/ or exp Crack Cocaine/**
	Mortality	Mortal$ or fatal$ or death$ **exp "DEATH AND DYING"/ or exp Mortality/ or exp Mortality Rate/**

* 'key-words' in lowercase, 'MeSH' terms in **bold** # 'key-words' in lowercase, 'EMTREE' terms in **bold** ^ 'key words' in lowercase, explode terms in **bold**

Number of articles identified from mortality searches

	Search terms		Database		
			EMBASE	Medline	PsycINFO
1.	ATS	+ mortality	4095	1177	356
2.	Cocaine	+mortality	1980	600	228

PRISMA flowchart of search strategy

Amphetamine mortality search

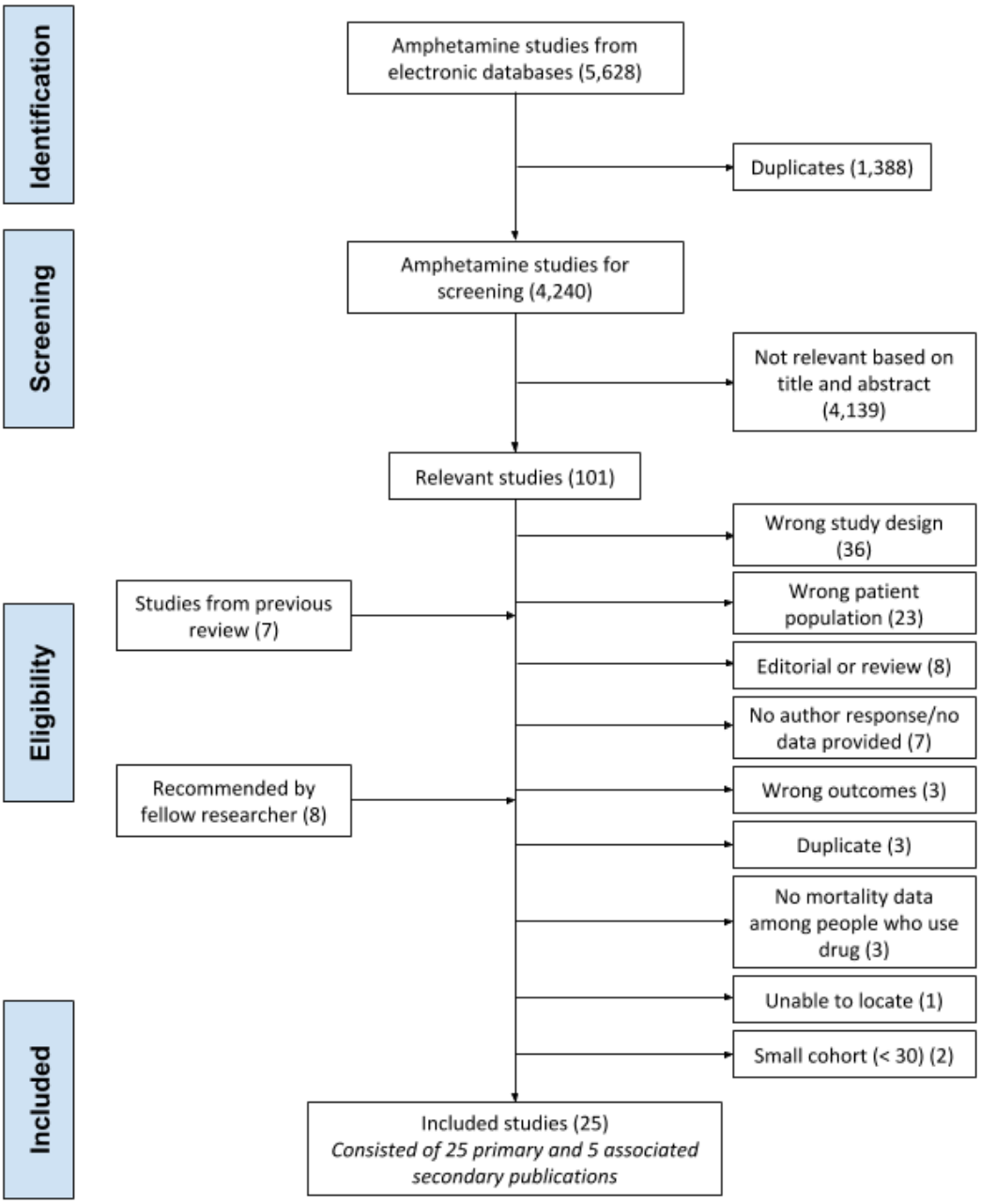

Figure G1. PRISMA flowchart showing selection of studies in the review of mortality among cohorts using amphetamines.

Cocaine mortality searches

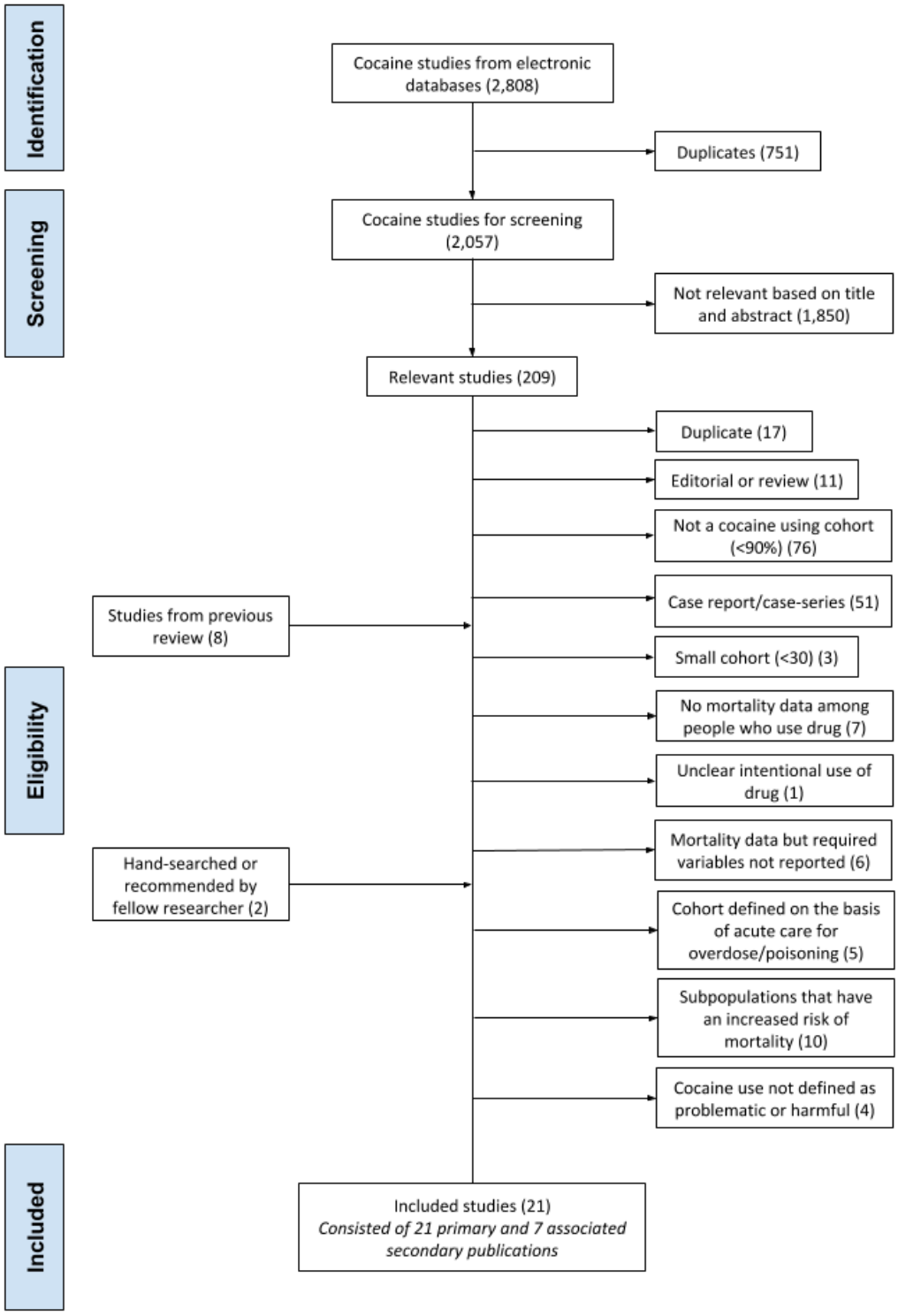

Figure G2. PRISMA flowchart showing selection of studies in the review of mortality among cohorts using cocaine.

List of studies included for each of the mortality reviews

Amphetamine

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Cocaine

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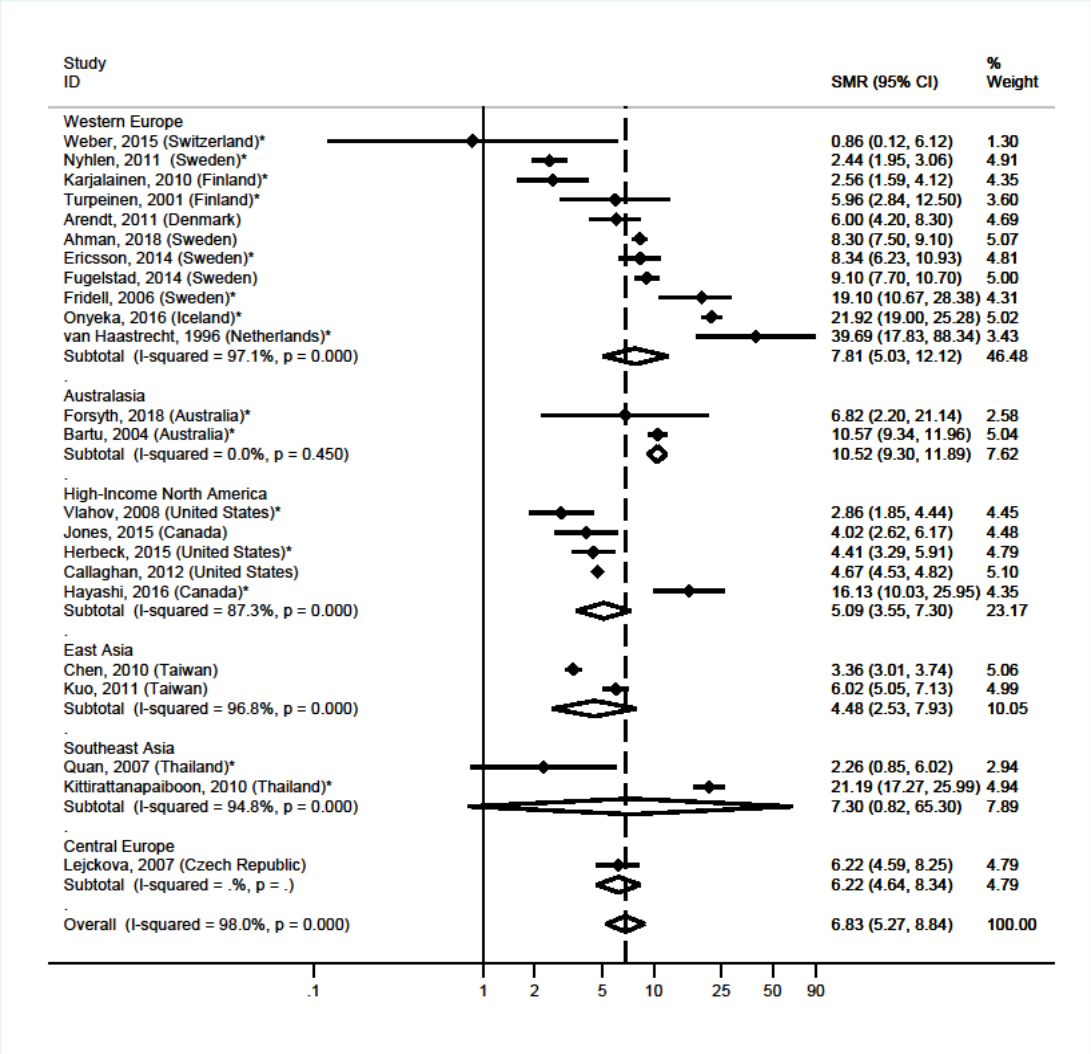


Figure E3. Forest plot displaying standardised mortality ratio (SMR) among cohorts of people who use amphetamines.

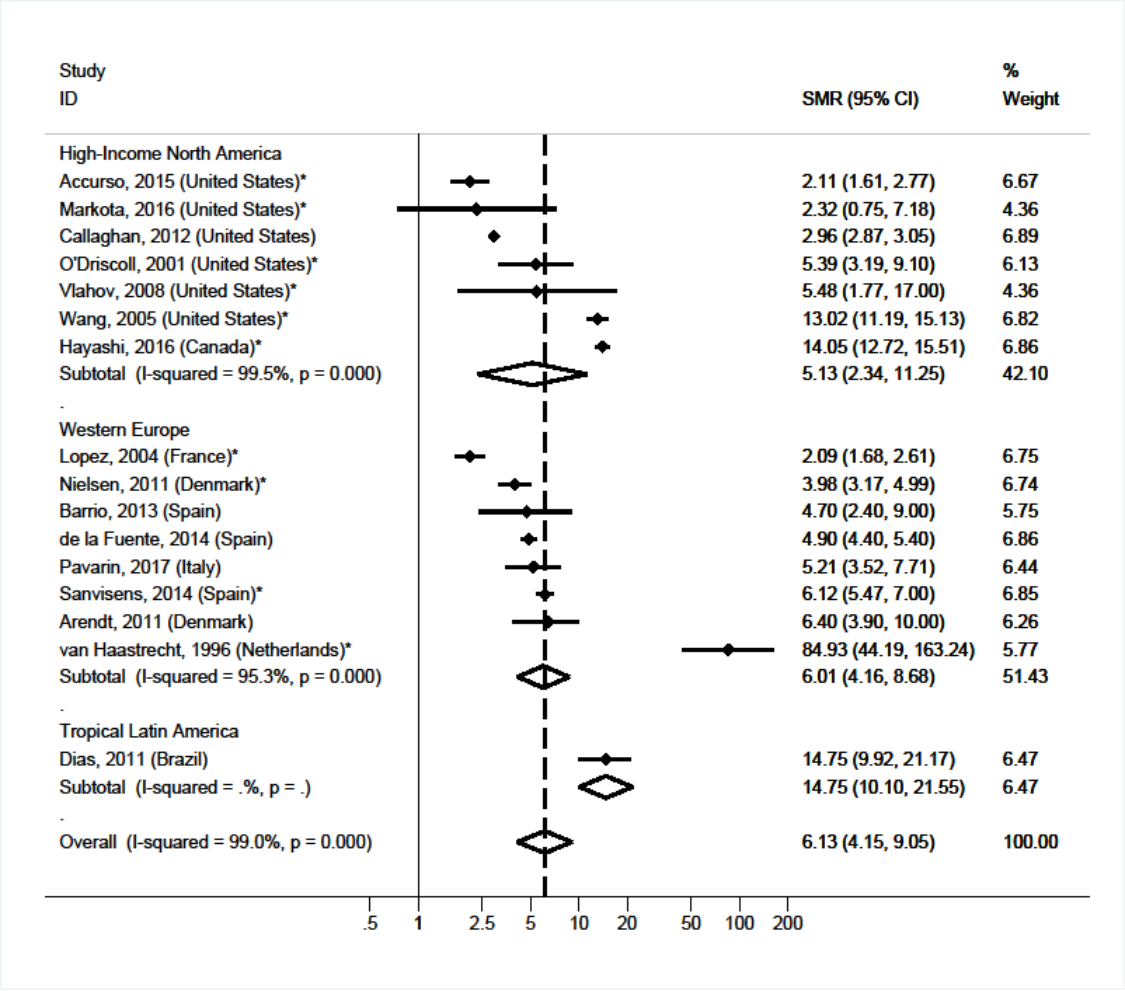


Figure E4. Forest plot displaying SMR among cohorts of people who use cocaine.

Webappendix H: Details of the mathematical modeling

Regional and global burden of mortality associated with stimulant dependence

To estimate the regional burden of mortality associated with stimulant dependence, we utilize a theoretical-minimum-risk exposure distribution[48] defined as the counterfactual status of the absence of stimulant dependence (which by definition has a relative risk of mortality of 1.0). Therefore, we use the associated equation for regional attributable fraction[48,49] (AF):

$$AF_i^j = \frac{P_i^j(SMR_i - 1)}{P_i^j(SMR_i - 1) + 1}$$

where *i* denotes the stimulant (cocaine or amphetamine), *j* is the GBD region (j=1…21), P is the regional age-standardized proportion of the population dependent on the stimulant, and SMR is the pooled standardized mortality ratio by stimulant type. For this analysis, we examine all-cause mortality, as well as cause-specific mortality due to suicide, accidental injury, cardiovascular, and homicide using SMRs from the review (**Table 2**).

We subsequently calculate the regional number of deaths associated with stimulant dependence by multiplying the region-specific AF_i with the region-specific numbers of deaths (M^j). We obtain region-specific numbers of deaths in 2017 from GBD data by all-cause, suicide (GBD category C.3.1. Self harm), accidental injuries (summing GBD categories C.1. Transport injuries and C.2. Unintentional Injuries), cardiovascular (B.2. Cardiovascular injuries), and homicide (C.3.2. Interpersonal violence).

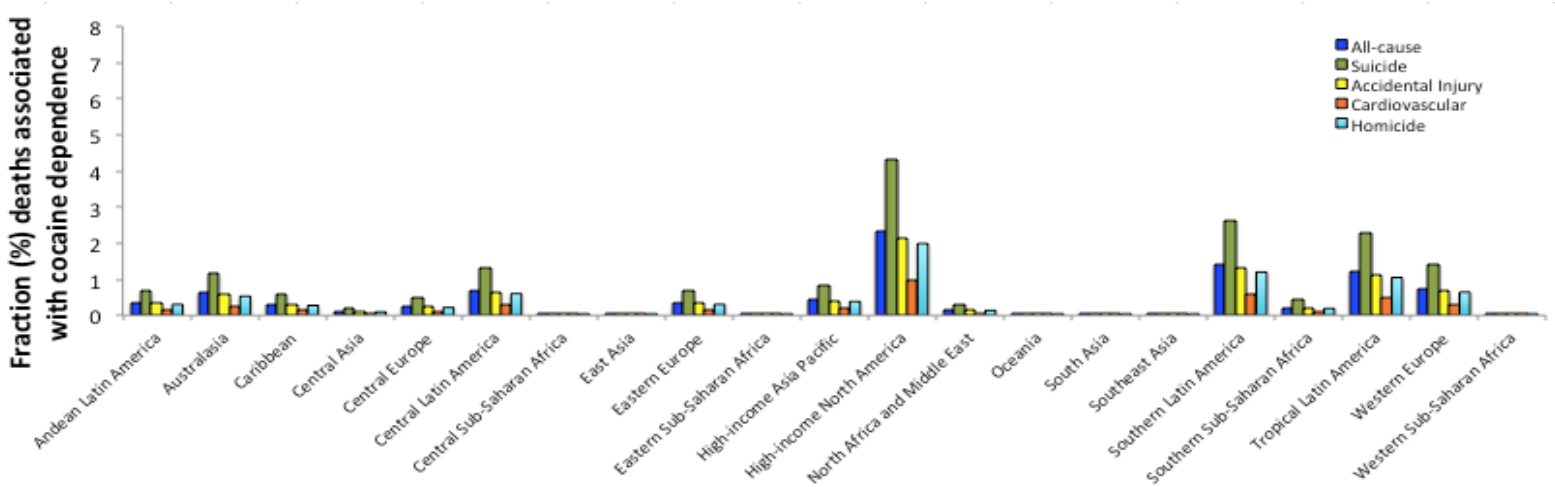
Due to uncertainty, we randomly sample 100,000 estimates from each parameter distribution. For the regional 2017 GBD data on stimulant dependence prevalence (per 100,000 population) we generate associated beta distributions. We randomly sample from lognormal distributions for the pooled SMR estimates from **Table 2** and from normal distributions for the regional 2017 GBD mortality data.

We perform calculations for each of the 21 GBD regions separately, and sum the deaths associated with stimulant dependence to generate a global estimate of excess mortality associated with each stimulant type. For each of the 100,000 simulations, the global fraction of deaths associated with stimulant dependence was then calculated by:

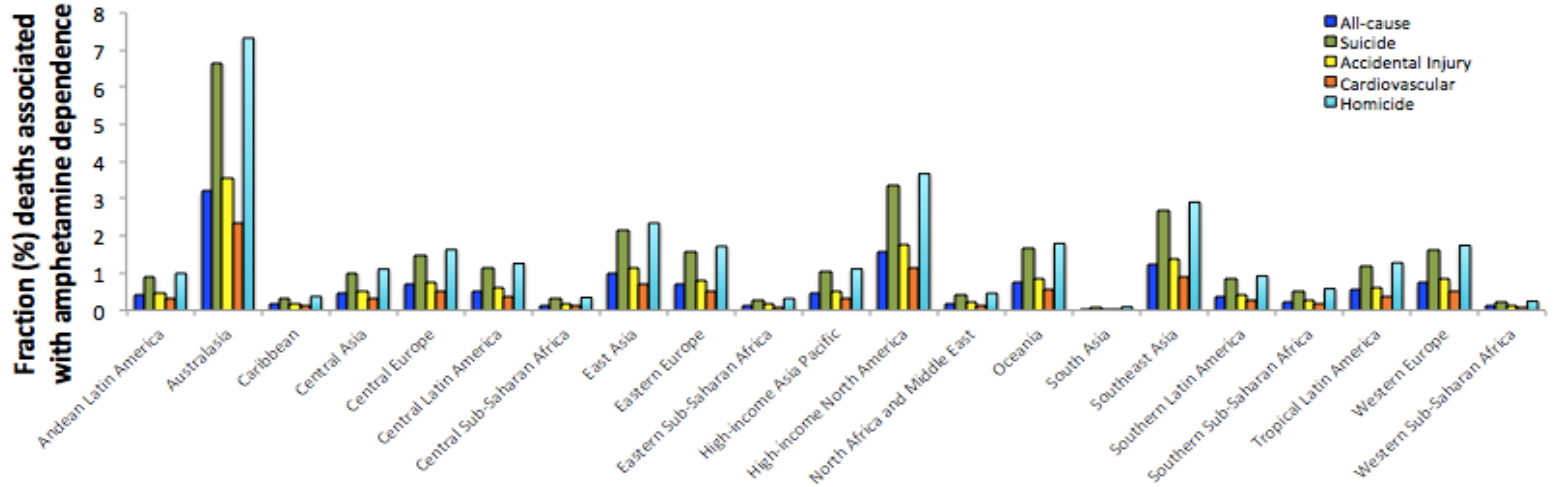
$$Global\ AF_i = \frac{\sum_{j=1}^{21} \frac{P_i^j(SMR_i - 1)}{P_i^j(SMR_i - 1) + 1} * M^j}{\sum_{j=1}^{21} M^j}$$

Figure H1: Fraction (%) of regional all-cause and cause-specific deaths associated with a) cocaine and b) amphetamine dependence in 2017.

1a. Fraction of deaths associated with cocaine dependence[†]



1b. Fraction of deaths associated with amphetamine dependence[†]



[†] Estimates derived from data from systematic reviews and GBD2017; for methods used to generate these estimates see webappendix H

Table H1. Regional and global attributable fraction (AF) and number of all-cause deaths associated with stimulant dependence in 2017.

	Amphetamine			Cocaine		
	Age-standardised rate per 100,000 (95%UI)	% AF all-cause mortality (95%UI)	Number all-cause deaths, in 1000's (95%UI)	Age-standardised rate per 100,000 (95%UI)	% AF all-cause mortality (95%UI)	Number all-cause deaths, in 1000's (95%UI)
Andean Latin America	77.2 (66.4-90.5)	0.42 (0.29-0.58)	1 (1-2)	79.4 (54.3-111.4)	0.36 (0.2-0.57)	1 (1-2)
Australasia	623.7 (537.0-702.4)	3.19 (2.26-4.34)	6 (5-9)	140.6 (121.1-163.1)	0.62 (0.4-0.9)	1 (1-2)
Caribbean	28.6 (21.9-36.6)	0.15 (0.10-0.22)	1 (0-1)	68.5 (59.3-79.5)	0.32 (0.21-0.47)	1 (1-2)
Central Asia	84.9 (61.3-115.2)	0.46 (0.29-0.69)	3 (2-4)	25.5 (21.7-30.0)	0.11 (0.07-0.17)	1 (0-1)
Central Europe	126.3 (97.5-162.5)	0.69 (0.45-0.99)	9 (6-13)	57.7 (49.5-67.0)	0.26 (0.17-0.37)	3 (2-5)
Central Latin America	97.8 (66.5-140.9)	0.53 (0.31-0.82)	7 (4-11)	159.5 (140.1-182.7)	0.71 (0.46-1.02)	10(6-14)
Central Sub-Saharan Africa	26.0 (19.6-34.2)	0.14 (0.09-0.21)	1 (1-2)	7.2 (5.9-8.6)	0.03 (0.02-0.05)	<1 (<1-<1)
East Asia	180.8 (122.8-255.8)	0.99 (0.59-1.52)	109 (65-168)	6.4 (5.2-7.9)	0.03 (0.02-0.04)	3 (2-5)
Eastern Europe	134.0 (97.5-178.7)	0.72 (0.46-1.08)	20 (13-30)	80.6 (70.7-91.7)	0.36 (0.23-0.52)	10 (6-14)
Eastern Sub-Saharan Africa	24.0 (18.2-31.3)	0.13 (0.08-0.19)	3 (2-5)	3.8 (3.0-4.7)	0.02 (0.01-0.03)	<1 (<1-1)
High-income Asia Pacific	85.7 (62.4-114.3)	0.46 (0.29-0.69)	8 (5-12)	102.0 (88.6-116.6)	0.45 (0.29-0.65)	8 (5-11)
High-income North America	296.9 (214.9-393.5)	1.56 (0.99-2.32)	49 (31-73)	539.2 (485.8-602.0)	2.34 (1.55-3.33)	74 (49-105)
North Africa and Middle East	35.8 (26.4-46.6)	0.19 (0.12-0.28)	5 (3-8)	35.9 (31.1-41.4)	0.16 (0.10-0.23)	5 (3-7)
Oceania	137.1 (92.2-197.4)	0.75 (0.44-1.18)	1 (0-1)	4.2 (3.3-5.4)	0.02 (0.01-0.03)	<1 (<1-<1)
South Asia	6.7 (5.0-8.7)	0.04 (0.02-0.05)	4 (3-7)	5.1 (4.2-6.3)	0.02 (0.01-0.03)	3 (2-4)
Southeast Asia	225.0 (147.9-326.0)	1.23 (0.72-1.93)	52 (31-82)	4.8 (3.8-5.9)	0.02 (0.01-0.03)	1 (1-1)
Southern Latin America	70.2 (48.9-97.4)	0.39 (0.3-0.59)	2 (1-3)	319.5 (284.6-363.2)	1.41 (0.93-2.02)	7 (4-10)
Southern Sub-Saharan Africa	44.0 (33.5-57.8)	0.24 (0.15-0.35)	2 (1-2)	50.4 (44.1-57.9)	0.22 (0.14-0.32)	1 (1-2)
Tropical Latin America	98.9 (66.7-141.9)	0.53 (0.31-0.83)	7 (4-12)	278.6 (245.6-318.0)	1.23 (0.81-1.76)	17 (11-24)
Western Europe	135.8 (99.8-180.3)	0.73 (0.46-1.09)	30 (19-45)	170.1 (153.0-191.6)	0.76 (0.50-1.08)	31 (21-45)
Western Sub-Saharan Africa	23.2 (17.4-30.0)	0.10 (0.06-0.15)	3 (2-5)	7.6 (6.4-8.8)	0.03 (0.02-0.05)	1 (1-2)
Global	95.9 (70.0-128.4)	0.58 (0.41-0.80)	326 (228-449)	63.7 (57.3-71.3)	0.32 (0.21-0.45)	178 (119-252)

Table H2. Regional and global attributable fraction (AF) associated with stimulant dependence in 2017.

	Amphetamines				Cocaine			
	% AF suicide mortality (95%UI)	% AF accidental injury mortality (95%UI)	% AF cardiovascular mortality (95%UI)	% AF homicide mortality (95%UI)	% AF suicide mortality (95%UI)	% AF accidental injury mortality (95%UI)	% AF cardiovascular mortality (95%UI)	% AF homicide mortality (95%UI)
Andean Latin America	0.91 (0.23-2.34)	0.47 (0.20-0.90)	0.30 (0.20-0.43)	0.99 (0.57-1.61)	0.67 (0.39-1.06)	0.33 (0.19-0.53)	0.15 (0.02-0.40)	0.30 (0.04-0.88)
Australasia	6.67 (1.81-15.90)	3.57 (1.55-6.69)	2.33 (1.56-3.28)	7.33 (4.35-11.38)	1.17 (0.78-1.67)	0.57 (0.37-0.83)	0.26 (0.03-0.66)	0.53 (0.07-1.50)
Caribbean	0.34 (0.08-0.89)	0.17 (0.07-0.34)	0.11 (0.07-0.17)	0.37 (0.20-0.62)	0.61 (0.40-0.87)	0.30 (0.19-0.43)	0.13 (0.01-0.34)	0.28 (0.04-0.77)
Central Asia	1.02 (0.25-2.66)	0.52 (0.21-1.04)	0.34 (0.20-0.52)	1.11 (0.59-1.89)	0.21 (0.14-0.31)	0.10 (0.07-0.15)	0.05 (0.01-0.12)	0.10 (0.01-0.28)
Central Europe	1.50 (0.38-3.86)	0.77 (0.32-1.51)	0.50 (0.31-0.74)	1.63 (0.90-2.71)	0.48 (0.32-0.69)	0.23 (0.15-0.34)	0.11 (0.01-0.27)	0.22 (0.03-0.62)
Central Latin America	1.15 (0.28-3.06)	0.59 (0.23-1.21)	0.38 (0.22-0.61)	1.26 (0.63-2.19)	1.33 (0.89-1.89)	0.65 (0.42-0.93)	0.29 (0.03-0.75)	0.60 (0.60-1.69)
Central Sub-Saharan Africa	0.31 (0.08-0.82)	0.16 (0.06-0.32)	0.10 (0.06-0.15)	0.34 (0.18-0.58)	0.06 (0.04-0.09)	0.03 (0.02-0.04)	0.01 (0-0.03)	0.03 (0-0.08)
East Asia	2.15 (0.52-5.58)	1.11 (0.44-2.26)	0.72 (0.41-1.13)	2.35 (1.21-4.05)	0.05 (0.04-0.08)	0.03 (0.02-0.04)	0.01 (0-0.03)	0.02 (0-0.07)
Eastern Europe	1.58 (0.39-4.09)	0.81 (0.33-1.62)	0.52 (0.32-0.80)	1.72 (0.92-2.90)	0.67 (0.45-0.96)	0.33 (0.21-0.47)	0.15 (0.02-0.38)	0.30 (0.04-0.86)
Eastern Sub-Saharan Africa	0.29 (0.07-0.76)	0.15 (0.06-0.29)	0.09 (0.06-0.14)	0.31 (0.17-0.53)	0.03 (0.02-0.05)	0.02 (0.01-0.02)	0.01 (0-0.02)	0.01 (0-0.04)
High-income Asia Pacific	1.02 (0.25-2.67)	0.52 (0.21-1.04)	0.34 (0.20-0.51)	1.11 (0.59-1.88)	0.85 (0.56-1.21)	0.41 (0.27-0.60)	0.19 (0.02-0.48)	0.38 (0.05-1.09)
High-income North America	3.36 (0.85-8.52)	1.75 (0.71-3.45)	1.14 (0.69-1.73)	3.67 (1.99-6.13)	4.33 (2.96-6.05)	2.15 (1.42-3.07)	0.98 (0.11-2.50)	1.99 (0.27-5.47)
North Africa and Middle East	0.42 (0.10-1.10)	0.21 (0.09-0.43)	0.14 (0.08-0.21)	0.46 (0.24-0.77)	0.30 (0.20-0.43)	0.15 (0.09-0.21)	0.07 (0.01-0.17)	0.14 (0.02-0.39)
Oceania	1.65 (0.40-4.32)	0.85 (0.33-1.73)	0.55 (0.31-0.87)	1.80 (0.91-3.14)	0.04 (0.02-0.05)	0.02 (0.01-0.03)	0.01 (0-0.02)	0.02 (0-0.05)
South Asia	0.08 (0.02-0.21)	0.04 (0.02-0.08)	0.03 (0.02-0.04)	0.09 (0.05-0.15)	0.04 (0.03-0.06)	0.02 (0.01-0.03)	0.01 (0-0.02)	0.02 (0-0.06)
Southeast Asia	2.66 (0.64-6.94)	1.38 (0.53-2.81)	0.89 (0.51-1.43)	2.91 (1.47-5.06)	0.04 (0.03-0.06)	0.02 (0.01-0.03)	0.01 (0-0.02)	0.02 (0-0.05)
Southern Latin America	0.85 (0.21-2.22)	0.43 (0.17-0.88)	0.28 (0.16-0.44)	0.92 (0.48-1.60)	2.63 (1.78-3.71)	1.30 (0.85-1.86)	0.59 (0.07-1.50)	1.20 (0.16-3.34)
Southern Sub-Saharan Africa	0.53 (0.13-1.39)	0.27 (0.11-0.54)	0.17 (0.11-0.26)	0.58 (0.31-0.97)	0.42 (0.28-0.60)	0.21 (0.13-0.30)	0.09 (0.01-0.24)	0.19 (0.03-0.54)
Tropical Latin America	1.17 (0.28-3.09)	0.60 (0.23-1.23)	0.39 (0.22-0.62)	1.28 (0.64-2.23)	2.29 (1.54-3.24)	1.13 (0.74-1.62)	0.51 (0.06-1.31)	1.05 (0.14-2.92)
Western Europe	1.60 (0.40-4.14)	0.82 (0.33-1.64)	0.53 (0.32-0.81)	1.74 (0.93-2.93)	1.42 (0.96-2.01)	0.69 (0.46-1.00)	0.31 (0.04-0.80)	0.65 (0.09-1.80)
Western Sub-Saharan Africa	0.22 (0.05-0.59)	0.11 (0.05-0.23)	0.07 (0.04-0.11)	0.24 (0.13-0.41)	0.06 (0.04-0.09)	0.03 (0.02-0.05)	0.01 (0-0.04)	0.03 (0-0.08)
Global	1.23 (0.32-3.08)	0.59 (0.25-1.14)	0.48 (0.32-0.69)	1.23 (0.71-1.96)	0.65 (0.44-0.90)	0.24 (0.16-0.33)	0.14 (0.02-0.35)	0.47 (0.06-1.31)

Details of HIV and HCV epidemic model among PWID

Model description

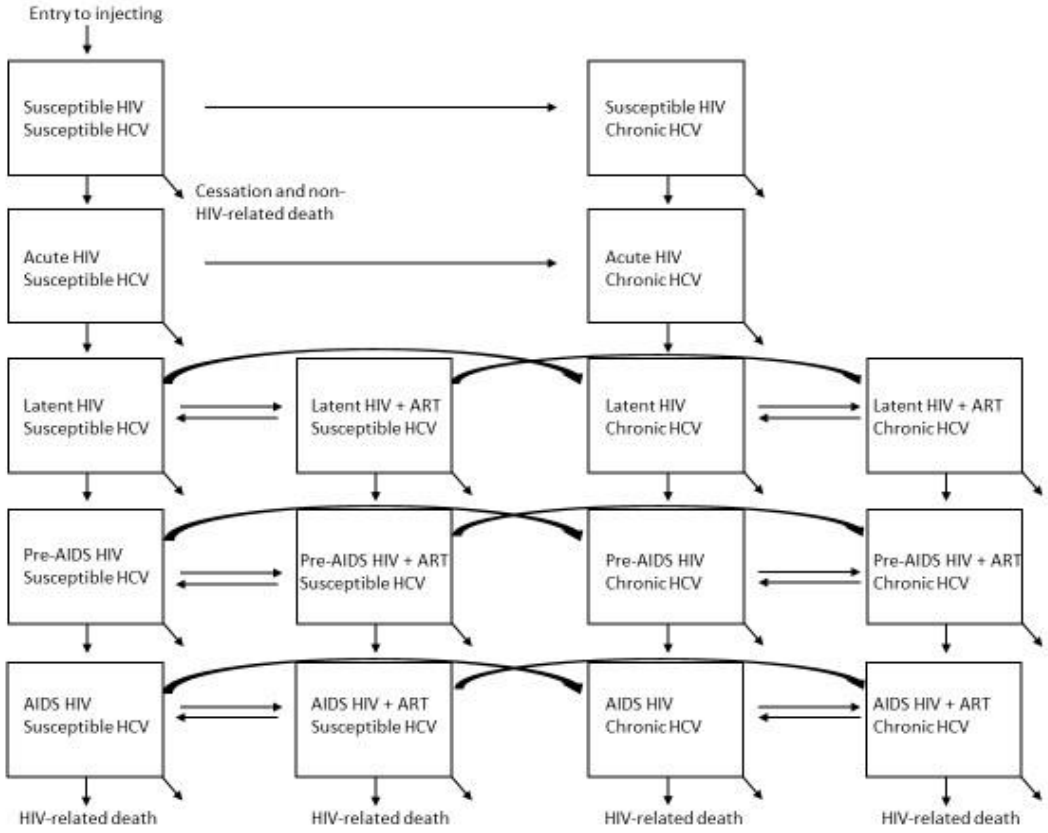
We developed a dynamic, deterministic compartmental joint model of HIV and HCV transmission among people who inject drugs (PWID) (see **Figure H1**). The model incorporated sexual and injecting-related transmission of HIV, and injecting-related transmission of HCV. We stratified the model by HIV and HCV infection status (including coinfection states), stimulant injection (yes/no), and intervention status for stimulant users (on/off). HIV status was stratified by disease stage (susceptible, acute, latent, pre-AIDS, AIDS) and ART status (latent on ART, pre-AIDS on ART, and AIDS on ART). After HIV infection, individuals enter a short period of acute infection (characterized by high viraemia), followed by a longer latent phase, followed by a pre-AIDS phase (of high viraemia) and AIDS phase (where we assume individuals do not engage in injecting or sexual activity and therefore do not contribute to transmission). Based on elevated viral loads, we assumed that individuals in the acute and pre-AIDS stages were more transmissible compared to the latent stage.[50,51] Individuals in the latent stage or later can be recruited on to and drop out of ART, which we assume reduces HIV progression rates, reduces HIV-related mortality from AIDS, reduces HIV sexual transmission, and reduces HIV injecting-related transmission (although to a lower and more uncertain extent). HCV infection was stratified by susceptible and chronic HCV infection. Based on very low HCV treatment rates among PWID (<1% treated globally), we did not incorporate HCV treatment; thus individuals with chronic HCV infection were assumed to remain chronically infected until death. We incorporate biological interactions between the infections; HIV infected individuals were less likely to spontaneously clear HCV infection[52], and individuals coinfected with HIV and HCV not receiving ART were assumed to more readily transmit HCV due to elevated viral loads.[53] The model was open such that that PWID could enter through initiation of injection drug use and leave the model through death or permanent cessation of injection drug use.

For our baseline analysis, PWID entered the model as either a stimulant injector or not and remained in that risk group (i.e. no turnover), but we examine the impact of turnover in a sensitivity analysis. We assume proportional mixing between all groups. Based on literature, we incorporate both elevated injecting and sexual risk among stimulant injectors compared to non-stimulant injectors[54]. The magnitude of these relative risks were allowed to vary, and calibrated to the observed differences in HIV incidence (due to elevated injecting and sexual risks) and HCV prevalence (due to elevated injecting risk) among stimulant injectors compared to those not injecting stimulants from the systematic review data. Stimulant using PWID could be recruited onto or drop off from an intervention (in this case, high coverage needle and syringe programs, NSP) to

reduce the injecting-related risks associated with stimulant injection (and was assumed to have no impact on sexual transmission).

Figure H2: Model schematic of HIV and HCV co-infection stages

(a)



Model Equations

PWID were defined by their HIV status (compartments *x,h,y,l,b,w,a,z* described in the following paragraph), HCV status (subscript *j, j*=0 for HCV susceptible, 1 for HCV chronically infected), and stimulant injecting status (superscript *i, i*=0 for no stimulant injection, 1 for stimulant injection). The rate of entry to injecting was defined by Ω where a proportion enter as PWID who inject stimulants ($p_{stimulant}$). Individuals susceptible to HIV (x_j^i) could become infected with HIV via parenteral or sexual exposure $\left(\lambda_{injHIV}^i + \lambda_{sex}^i\right)$ and move into the acute HIV compartment (h_j^i) followed by the latent HIV phase (y_j^i) where they could be recruited onto ART at a rate α or drop off ART at a rate δ. If not on ART, individuals progressed from the latent phase to the pre-AIDS phase (b_j^i) and then AIDS phase (a_j^i). From the AIDS phase they could die of HIV-related causes at rate θ. If on latent phase

ART (l_j^i) or pre-AIDS ART (w_j^i), progression was reduced by a factor ν compared to those off ART. If on AIDS phase ART (z_j^i), HIV-related mortality was reduced by a factor ρ. PWID could exit through either background mortality (μ_1) or injection cessation (μ_2). HIV negative PWID who acquired HCV through parenteral exposure was defined as the proportion of HIV negative PWID who did not spontaneously clear the virus (ϵ) multiplied by the force of infection for HCV, λ_{injHCV}^i. If HIV-positive, the proportion of PWID who did not spontaneously clear the virus was defined as ϑ. PWID who injected stimulants could be recruited onto an intervention (high coverage NSP) at rate η and drop off the intervention at rate ζ (defined by compartments with capital letters, *X, H, Y, L, B, W, A, Z*).

For HCV susceptible PWID who do not inject stimulants:

$$\frac{dx_0^0}{dt} = \Omega(1 - p_{stimulant}) - x_0^0(\lambda_{injHIV}^0 + \lambda_{sex}^0) - x_0^0(\mu_1 + \mu_2) - \epsilon x_0^0 \lambda_{injHCV}^0$$

$$\frac{dh_0^0}{dt} = x_0^0(\lambda_{injHIV}^0 + \lambda_{sex}^0) - \gamma h_0^0 - h_0^0(\mu_1 + \mu_2) - \vartheta h_0^0 \lambda_{injHCV}^0$$

$$\frac{dy_0^0}{dt} = \gamma h_0^0 - \kappa y_0^0 + \delta \; l_0^0 - \alpha y_0^0 - y_0^0(\mu_1 + \mu_2) - \vartheta y_0^0 \lambda_{injHCV}^0$$

$$\frac{dl_0^0}{dt} = y_0^0 + \alpha y_0^0 - \nu\kappa l_0^0 - \delta l_0^0 - l_0^0(\mu_1 + \mu_2) - \vartheta l_0^0 \lambda_{injHCV}^0$$

$$\frac{db_0^0}{dt} = \kappa y_0^0 + \delta w_0^0 - \alpha b_0^0 - \tau b_0^0 - b_0^0(\mu_1 + \mu_2) - \vartheta b_0^0 \lambda_{injHCV}^0$$

$$\frac{dw_0^0}{dt} = \nu\kappa l_0^0 + \alpha b_0^0 - \delta w_0^0 - \nu\tau w_0^0 - w_0^0(\mu_1 + \mu_2) - \vartheta w_0^0 \lambda_{injHCV}^0$$

$$\frac{da_0^0}{dt} = \tau b_0^0 + \delta z_0^0 - \alpha a_0^0 - \theta a_0^0 - a_0^0(\mu_1 + \mu_2) - \vartheta a_0^0 \lambda_{injHCV}^0$$

$$\frac{dz_0^0}{dt} = \nu\tau w_0^0 + \alpha a_0^0 - \delta z_0^0 - \rho\theta z_0^0 - z_0^0(\mu_1 + \mu_2) - \vartheta z_0^0 \lambda_{injHCV}^0$$

For HCV chronically infected PWID who do not inject stimulants:

$$\frac{dx_1^0}{dt} = x_1^0(\lambda_{injHIV}^0 + \lambda_{sex}^0) - x_1^0(\mu_1 + \mu_2) + \epsilon x_0^0 \lambda_{injHCV}^0$$

$$\frac{dh_1^0}{dt} = x_1^0(\lambda_{injHIV}^0 + \lambda_{sex}^0) - \gamma h_1^0 - h_1^0(\mu_1 + \mu_2) + \vartheta h_0^0 \lambda_{injHCV}^0$$

$$\frac{dy_1^0}{dt} = \gamma h_1^0 - \kappa y_1^0 + \delta l_1^0 - \alpha y_1^0 - y_1^0(\mu_1 + \mu_2) + \vartheta y_0^0 \lambda_{injHCV}^0$$

$$\frac{dl_1^0}{dt} = \alpha y_1^0 - \nu\kappa l_1^0 - \delta l_1^0 - l_1^0(\mu_1 + \mu_2) + \vartheta l_0^0 \lambda_{injHCV}^0$$

$$\frac{db_1^0}{dt} = \kappa y_1^0 + \delta w_1^0 - \alpha b_1^0 - \tau b_1^0 - b_1^0(\mu_1 + \mu_2) + \vartheta b_0^0 \lambda_{injHCV}^0$$

$$\frac{dw_1^0}{dt} = \nu\kappa l_1^0 + \alpha b_1^0 - \delta w_1^0 - \nu\tau w_1^0 - w_1^0(\mu_1 + \mu_2) + \vartheta w_0^0 \lambda_{injHCV}^0$$

$$\frac{da_1^0}{dt} = \tau b_1^0 + \delta z_1^0 - \alpha a_1^0 - \theta a_1^0 - a_1^0(\mu_1 + \mu_2) + \vartheta a_0^0 \lambda_{injHCV}^0$$

$$\frac{dz_1^0}{dt} = \nu\tau w_1^0 + \alpha a_1^0 - \delta z_1^0 - \rho\theta z_1^0 - z_1^0(\mu_1 + \mu_2) + \vartheta z_0^0 \lambda_{injHCV}^0$$

For HCV susceptible PWID who inject stimulants off NSP:

$$\frac{dx_0^1}{dt} = \Omega(t) p_{stimulant} + \zeta x_0^1 - x_0^1\left(\lambda_{injHIV}^1 + \lambda_{sex}^1\right) - x_0^1(\mu_1 + \mu_2) - \epsilon x_0^1 \lambda_{injHCV}^1 - \eta x_0^1$$

$$\frac{dh_0^1}{dt} = x_0^1\left(\lambda_{injHIV}^1 + \lambda_{sex}^1\right) + \zeta h_0^1 - \gamma h_0^1 - h_0^1(\mu_1 + \mu_2) - \vartheta h_0^1 \lambda_{injHCV}^1 - \eta h_0^1$$

$$\frac{dy_0^1}{dt} = \gamma h_0^1 + \zeta y_0^1 - \kappa y_0^1 + \delta_k l_0^1 - \alpha y_0^1 - y_0^1(\mu_1 + \mu_2) - \vartheta y_0^1 \lambda_{injHCV}^1 - \eta y_0^1$$

$$\frac{dl_0^1}{dt} = \alpha y_0^1 + \zeta l_0^1 - \nu\kappa l_0^1 - \delta l_0^1 - l_0^1(\mu_1 + \mu_2) - \vartheta l_0^1 \lambda_{injHCV}^1 - \eta l_0^1$$

$$\frac{db_0^1}{dt} = \kappa y_0^1 + \zeta b_0^1 + \delta w_0^1 - \alpha b_0^1 - \tau b_0^1 - b_0^1(\mu_1 + \mu_2) - \vartheta b_0^1 \lambda_{injHCV}^1 - \eta b_0^1$$

$$\frac{dw_0^1}{dt} = \nu\kappa l_0^1 + \zeta w_0^1 + \alpha b_0^1 - \delta w_0^1 - \nu\tau w_0^1 - w_0^1(\mu_1 + \mu_2) - \vartheta w_0^1 \lambda_{injHCV}^1 - \eta w_0^1$$

$$\frac{da_0^1}{dt} = \tau b_0^1 + \zeta a_0^1 + \delta z_0^1 - \alpha a_0^1 - \theta a_0^1 - a_0^1(\mu_1 + \mu_2) - \vartheta a_0^1 \lambda_{injHCV}^1 - \eta a_0^1$$

$$\frac{dz_0^1}{dt} = \nu\tau w_0^1 + \zeta z_0^1 + \alpha a_0^1 - \delta z_0^1 - \rho\theta z_0^1 - z_0^1(\mu_1 + \mu_2) - \vartheta z_0^1 \lambda_{injHCV}^1 - \eta z_0^1$$

For HCV chronically infected PWID who inject stimulants off NSP:

$$\frac{dx_1^1}{dt} = \zeta x_1^1 - x_1^1\left(\lambda_{injHIV}^1 + \lambda_{sex}^1\right) - x_1^1(\mu_1 + \mu_2) + \epsilon x_0^1 \lambda_{injHCV}^1 - \eta x_1^1$$

$$\frac{dh_1^1}{dt} = x_1^1\left(\lambda_{injHIV}^1 + \lambda_{sex}^1\right) + \zeta h_1^1 - \gamma h_1^1 - h_1^1(\mu_1 + \mu_2) + \vartheta h_0^1 \lambda_{injHCV}^1 - \eta h_1^1$$

$$\frac{dy_1^1}{dt} = \gamma h_1^1 + \zeta y_1^1 - \kappa y_1^1 + \delta_k l_1^1 - \alpha y_1^1 - y_1^1(\mu_1 + \mu_2) + \vartheta y_0^1 \lambda_{injHCV}^1 - \eta y_1^1$$

$$\frac{dl_1^1}{dt} = \alpha y_1^1 + \zeta l_1^1 - \nu\kappa l_1^1 - \delta l_1^1 - l_1^1(\mu_1 + \mu_2) + \vartheta l_0^1 \lambda_{injHCV}^1 - \eta l_1^1$$

$$\frac{db_1^1}{dt} = \kappa y_1^1 + \zeta b_1^1 + \delta w_1^1 - \alpha b_1^1 - \tau b_1^1 - b_1^1(\mu_1 + \mu_2) + \vartheta b_0^1 \lambda_{injHCV}^1 - \eta b_1^1$$

$$\frac{dw_1^1}{dt} = \nu\kappa l_1^1 + \zeta w_1^1 + \alpha b_1^1 - \delta w_1^1 - \nu\tau w_1^1 - w_1^1(\mu_1 + \mu_2) + \vartheta w_0^1 \lambda_{injHCV}^1 - \eta w_1^1$$

$$\frac{da_1^1}{dt} = \tau b_1^1 + \zeta a_1^1 + \delta z_1^1 - \alpha a_1^1 - \theta a_1^1 - a_1^1(\mu_1 + \mu_2) + \vartheta a_0^1 \lambda_{injHCV}^1 - \eta a_1^1$$

$$\frac{dz_1^1}{dt} = \nu\tau w_1^1 + \zeta z_1^1 + \alpha a_1^1 - \delta z_1^1 - \rho\theta z_1^1 - z_1^1(\mu_1 + \mu_2) + \vartheta z_0^1 \lambda_{injHCV}^1 - \eta z_1^1$$

For HCV susceptible PWID who inject stimulants on NSP:

$$\frac{dX_0^1}{dt} = -\zeta X_0^1 - X_0^1\left(\lambda_{injHIV\_NSP}^1 + \lambda_{sex}^1\right) - X_0^1(\mu_1 + \mu_2) - \epsilon X_0^1 \lambda_{injHCV\_NSP}^1 + \eta X_0^1$$

$$\frac{dH_0^1}{dt} = X_0^1\left(\lambda_{injHIV\_NSP}^1 + \lambda_{sex}^1\right) - \zeta H_0^1 - \gamma H_0^1 - H_0^1(\mu_1 + \mu_2) - \vartheta H_0^1 \lambda_{injHCV\_NSP}^1 + \eta H_0^1$$

$$\frac{dY_0^1}{dt} = \gamma H_0^1 - \zeta y_0^1 - \kappa Y_0^1 + \delta L_0^1 - \alpha Y_0^1 - Y_0^1(\mu_1 + \mu_2) - \vartheta Y_0^1 \lambda_{injHCV\_NSP}^1 + \eta Y_0^1$$

$$\frac{dL_0^1}{dt} = \alpha Y_0^1 - \zeta L_0^1 - \nu\kappa L_0^1 - \delta L_0^1 - L_0^1(\mu_1 + \mu_2) - \vartheta L_0^1 \lambda_{injHCV\_NSP}^1 + \eta L_0^1$$

$$\frac{dB_0^1}{dt} = \kappa Y_0^1 - \zeta B_0^1 + \delta W_0^1 - \alpha B_0^1 - \tau B_0^1 - B_0^1(\mu_1 + \mu_2) - \vartheta B_0^1 \lambda_{injHCV\_NSP}^1 + \eta B_0^1$$

$$\frac{dW_0^1}{dt} = \nu\kappa L_0^1 - \zeta W_0^1 + \alpha B_0^1 - \delta W_0^1 - \nu\tau W_0^1 - W_0^1(\mu_1 + \mu_2) - \vartheta W_0^1 \lambda_{injHCV\_NSP}^1 + \eta W_0^1$$

$$\frac{dA_0^1}{dt} = \tau B_0^1 - \zeta A_0^1 + \delta Z_0^1 - \alpha A_0^1 - \theta A_0^1 - A_0^1(\mu_1 + \mu_2) - \vartheta A_0^1 \lambda_{injHCV\_NSP}^1 + \eta A_0^1$$

$$\frac{dZ_0^1}{dt} = \nu\tau W_0^1 - \zeta Z_0^1 + \alpha A_0^1 - \delta Z_0^1 - \rho\theta Z_0^1 - Z_0^1(\mu_1 + \mu_2) - \vartheta Z_0^1 \lambda_{injHCV\_NSP}^1 + \eta Z_0^1$$

For HCV chronically infected PWID who inject stimulants on NSP:

$$\frac{dX_1^1}{dt} = \eta X_1^1 - \zeta X_1^1 - X_1^1\left(\lambda_{injHIV\_NSP}^1 + \lambda_{sex}^1\right) - X_1^1(\mu_1 + \mu_2) + \epsilon X_0^1 \lambda_{injHCV\_NSP}^1$$

$$\frac{dH_1^1}{dt} = X_1^1\left(\lambda_{injHIV\_NSP}^1 + \lambda_{sex}^1\right) - \zeta H_1^1 - \gamma H_1^1 - H_1^1(\mu_1 + \mu_2) + \vartheta H_0^1 \lambda_{injHCV_{NSP}}^1 + \eta H_1^1$$

$$\frac{dY_1^1}{dt} = \gamma H_1^1 - \zeta Y_1^1 - \kappa Y_1^1 + \delta_k L_1^1 - \alpha Y_1^1 - Y_1^1(\mu_1 + \mu_2) + \vartheta Y_0^1 \lambda_{injHCV_{NSP}}^1 + \eta Y_1^1$$

$$\frac{dL_1^1}{dt} = \alpha Y_1^1 - \zeta L_1^1 - \nu\kappa L_1^1 - \delta L_1^1 - L_1^1(\mu_1 + \mu_2) + \vartheta L_0^1 \lambda_{injHCV_{NSP}}^1 + \eta L_1^1$$

$$\frac{dB_1^1}{dt} = \kappa Y_1^1 - \zeta B_1^1 + \delta W_1^1 - \alpha B_1^1 - \tau B_1^1 - B_1^1(\mu_1 + \mu_2) + \vartheta B_0^1 \lambda_{injHCV_{NSP}}^1 + \eta B_1^1$$

$$\frac{dW_1^1}{dt} = \nu\kappa L_1^1 - \zeta W_1^1 + \alpha B_1^1 - \delta W_1^1 - \nu\tau W_1^1 - W_1^1(\mu_1 + \mu_2) + \vartheta W_0^1 \lambda_{injHCV_{NSP}}^1 + \eta W_1^1$$

$$\frac{dA_1^1}{dt} = \tau B_1^1 - \zeta A_1^1 + \delta Z_1^1 - \alpha A_1^1 - \theta A_1^1 - A_1^1(\mu_1 + \mu_2) + \vartheta A_0^1 \lambda_{injHCV_{NSP}}^1 + \eta A_1^1$$

$$\frac{dZ_1^1}{dt} = \nu\tau W_1^1 - \zeta Z_1^1 + \alpha A_1^1 - \delta Z_1^1 - \rho\theta Z_1^1 - Z_1^1(\mu_1 + \mu_2) + \vartheta Z_0^1 \lambda_{injHCV_{NSP}}^1 + \eta Z_1^1$$

Entry into the PWID population is defined as:

$$\Omega(t) = (\mu_1 + \mu_2)N_1$$

where $\mu_1 + \mu_2$ represent the background mortality rate and injection cessation rate, respectively. The total population size is denoted by N_1.

Force of infection - HIV

The force of infection for HIV incorporated both injecting-related ($\lambda^i{}_{injHIV}$) and sexual transmission ($\lambda^i{}_{sex}$). The injecting forces of infection for HIV are defined by the equations below, assuming proportional sexual and injecting mixing. HIV transmissibility was increased for individuals in the acute phase (by a factor ε) and the pre-AIDS phase (by a factor ι) compared to the latent phase. Individuals on ART had reduced HIV injecting-related transmissibility (by a factor ω_{inj}) and sexual transmissibility (by a factor ω_{sex}) compared to those not on ART. PWID who inject stimulants experience increased risks of receptive syringe sharing and unprotected sex (RR_{inj} and RR_{sex}. respectively) compared to those who do not inject stimulants. The HIV injection infection rate (β_{injHIV}) was calculated by multiplying the HCV injection infection rate (β_{injHCV}) and the relative transmissability of HIV compared to HCV (σ). Individuals on NSP were associated with reduced risk of injecting-related HIV infection and transmission (RR_{NSPHIV}) compared to those off NSP. As such, the injecting-related HIV force of infection was constructed by multiplying the HIV injection infection rate (β_{injHIV}) by the risk-weighted HCV prevalence.

Therefore, the injecting-related HIV force of infection for PWID who do not inject stimulants was defined as:

$$\lambda^0{}_{injHIV} = \beta_{injHIV}\left[\frac{\Pi^0 + RR_{inj}\Pi^1}{\Gamma^0 + RR_{inj}\Gamma^1)}\right]$$

where

$$\Pi^i = \varepsilon h_j^i + y_j^i + \iota b_j^i + \omega_{inj}\left(l_j^i + w_j^i + z_j^i\right) + RR_{NSPHIV}\left(\varepsilon H_j^i + Y_j^i + \iota B_j^i + \omega_{inj}\left(L_j^i + W_j^i + Z_j^i\right)\right)$$

$$\Gamma^i = (x_j^i + h_j^i + y_j^i + l_j^i + b_j^i + w_j^i + z_j^i + RR_{NSPHIV}(X_j^i + H_j^i + Y_j^i + L_j^i + B_j^i + W_j^i + Z_j^i))$$

and

$\beta_{injHIV} = \sigma\beta_{injHCV}$.

For PWID who inject stimulants not on NSP:

$$\lambda^1{}_{injHIV} = RR_{inj}\lambda^0{}_{injHIV}$$

For PWID who inject stimulants on NSP:

$$\lambda^1{}_{injHIV\_NSP} = RR_{inj}RR_{NSPHIV}\lambda^0{}_{injHIV}$$

The sexual force of infection for HIV was defined as the following for PWID who do not inject stimulants:

$$\lambda^0{}_{sex} = \beta_{sex}\left[\frac{\varepsilon\left(h_j^0 + H_j^0 + RR_{sex}[h_j^1 + H_j^1]\right) + y_j^0 + Y_j^0 + RR_{sex}[y_j^1 + Y_j^1] + \iota\left(b_j^0 + B_j^0 + RR_{sex}[b_j^1 + B_j^1]\right) + \omega_{sex}\left(l_j^0 + L_j^0 + w_j^0 + W_j^0 + z_j^0 + Z_j^0 + RR_{sex}(l_j^1 + w_j^1 + z_j^1 + L_j^1 + W_j^1 + Z_j^1)\right)}{N_0}\right]$$

where N_0 denotes the total population excluding individuals with AIDS not on ART.

The sexual force of infection for HIV was defined as the following for PWID who inject stimulants:

$$\lambda^1{}_{sex} = RR_{sex}\lambda^0{}_{sex}$$

Force of infection - HCV

We incorporated injecting related HCV transmission, assuming proportional mixing. HIV-infected individuals not on ART had increased HCV transmissability by a factor of ϕ compared to HIV-negative individuals due to higher viral loads.[53] Individuals on NSP were associated with reduced risk of injecting-related HCV infection and transmission (RR_{NSPHCV}) compared to those off NSP.

For PWID who do not inject stimulants:

$$\lambda^0_{j\ injHCV} = \beta_{injHCV}\left[\frac{\Delta^0 + RR_{inj}\Delta^1}{\psi^0 + RR_{inj}\psi^1)}\right]$$

where

$$\Delta^i = x_1^i + h_1^i + y_1^i + b_1^i + \varphi\left(l_1^i + w_1^i + z_1^i\right) + RR_{NSPHCV}\left(X_1^i + H_1^i + Y_j^i + B_1^i + \varphi\left(L_1^i + W_1^i + Z_1^i\right)\right)$$

$$\psi^i = (x_j^i + h_j^i + y_j^i + l_j^i + b_j^i + w_j^i + z_j^i + RR_{NSPHCV}\left(X_j^i + H_j^i + Y_j^i + B_j^i + L_j^i + W_j^i + Z_j^i\right)).$$

For PWID who inject stimulants not on NSP:

$$\lambda^1_{j\ injHCV} = RR_{inj}\lambda^0_{j\ injHCV}$$

For PWID who inject stimulants on NSP:

$$\lambda^1_{j\ injHCV\_NSP} = RR_{inj}RR_{NSPHCV}\lambda^0_{j\ injHCV}$$

Model calibration and parameterization

We modeled three illustrative scenarios with varying levels of stimulant injection and differing epidemics of HIV and HCV among PWID: a setting with low prevalence (~15%) of amphetamine injecting (St. Petersburg-like), a setting with moderate prevalence (~35%) of cocaine injecting (Montreal-like), and a setting with high prevalence (~65%) of methamphetamine injecting (Bangkok-like). These illustrative scenarios were chosen to represent a range of settings with varied stimulant injection, and also because they have published associations between stimulant injecting and HIV and/or HCV among PWID. Montreal and Bangkok have very low HIV incidence (<1 per 100py) whereas Russia has higher HIV incidence among PWID (~7 per 100py). All settings have high chronic HCV prevalence (55-75%), so we additionally examined a sensitivity analysis with lower HCV (25%). The goal of the modeling exercise was not to conduct setting-specific modeling but rather to illustrate the potential contribution of stimulant injection on transmission of HIV and HCV in scenarios with different stimulant and epidemic characteristics. The values used in the calibration and parameterization of the models are found in **Table H3** and **Table H4**, respectively.

For each setting, we used Latin Hypercube Sampling to generate 500 parameter sets from uncertainty distributions, except for specific parameters used to calibrate the model.

For each parameter set, the model was calibrated at steady state to scenario-specific values for HIV incidence, HCV prevalence, ART coverage among HIV+ PWID, the proportion of incident HIV infections due to sexual transmission, as well as global systematic review data on increased risk of HIV infection among PWID who inject stimulants compared to PWID who do not inject stimulants (amphetamine incidence rate ratio [IRR]: 3.0, 95% CI: 2.2-4.1 and cocaine IRR: 3.6, 95% CI: 2.8-4.7,

Table I1) and increased odds of prevalent HCV infection among PWID who inject stimulants compared to PWID who do not inject stimulants (amphetamine odds ratio [OR]: 2.43, 95% CI: 1.33-4.43 and cocaine OR:2.92, 95% CI: 2.50-3.40, **Table I1**). Due to the underlying uncertainty in the increased risk of HIV and odds of HCV infection among PWID who inject stimulants obtained from the global review, we calibrated to sampled values for these parameters to generate simulations representing the range of possible uncertainty. This calibration was achieved through varying the HCV transmission rate, a proportion multiplied by the HCV transmission rate used to calculate HIV injection transmission rate (due to the reduced injection-related transmissibility of HIV compared to HCV), the HIV sexual transmission rate, the ART recruitment rate, the recruitment rate onto stimulant injection, the rate ratio of HIV incidence of PWID who inject stimulants compared to PWID who do not inject stimulants, and the odds ratio of chronic HCV prevalence of PWID who inject stimulants compared to PWID who do not inject stimulants. The model was calibrated using a global optimization solver (*fmincon* with *multistart* in MATLAB) by minimizing the sum log-likelihood of the calibration values given the data. We accepted fits in which the model projections were within the 95% CI of the observed HIV incidence data and within the 99% CI of the incidence rate ratio of HIV transmission and odds ratio of HCV prevalence among PWID who inject stimulants compared to PWID who do not inject stimulants.

As our primary goal was to compare the potential effect of stimulant injection on HIV and HCV epidemics among PWID across illustrative settings, although the calibration data (detailed above) varied, input parameters were identical across settings (**Table H4**). The exception to this was the upper uncertainty bound for duration of injection in St. Petersburg, where we increased the upper 95% confidence bound to 30 years (compared to 20 years in other settings) based on evidence that injecting duration could be longer in this setting and to be consistent with previous modeling[55].

Effect of ART on injecting-related transmissibility. The effect of ART on reducing injection-related transmissibility is highly uncertain, with empirical studies suggesting that ART can reduce HIV incidence among PWID but with uncertain magnitude of effect[56,57]. A recent HIV/HCV coinfection modeling analysis of Vancouver data produced an uncertain ART efficacy for reducing injection-related infectivity (44%, 95%CI 0-96%)[58]. Similarly uncertain estimates were obtained in the HIV pre-exposure prophylaxis trial among PWID in Bangkok, which found a 48.9% reduction (95%CI 9.6-72.2) in HIV incidence for those on PrEP[59]. Given these uncertain data for PWID, we chose a lower and more uncertainty effect of ART in reducing injecting-related transmissibility (median estimate 50%, sampled uniformly from 25-75%), compared to sexual transmissibility.

Table H3: Model calibration values

Calibration parameter	Calibration value			Sampling distribution	Reference (S: St Petersburg, M: Montreal, B: Bangkok)
	High stimulant injecting scenario (Bangkok-like)	Moderate stimulant injecting scenario (Montreal-like)	Low stimulant injecting scenario (St. Petersburg-like)		
Primary stimulant injected	Methamphetamine	Cocaine	Amphetamine type stimulant		
Proportion PWID who inject stimulants	65%	34%	13%		S: [60] M: 2017 data from Saint-Luc and HEPCO cohorts[61] B: [62]
HIV incidence among PWID	0.7 per 100 PY	0.3 per 100 PY	7.2 per 100 PY		S: [60] M: 2017 data from Saint-Luc and HEPCO cohorts[61] B: [59]
HCV chronic prevalence among PWID	74%	55%	75%		S: [63] M: 2017 data from Saint-Luc and HEPCO cohorts[61] B: [64] seroprevalence adjusted by spontaneous clearance and HIV status
ART coverage among HIV-infected PWID	55%	87%	11%		S: [65] M: 2017 data from Saint-Luc and HEPCO cohorts[61] B: [66]
HIV incidence if inject stimulants compared to HIV incidence if not inject stimulants	IRR 3.0 (95%CI 2.2-4.1) for amphetamines	IRR 3.6 (95%CI 2.8 to 4.7) for cocaine	IRR 3.0 (95%CI 2.2 to 4.1) for amphetamines	Lognormal	**Table I1** of this manuscript, based on primary class of stimulant injected[54]
Odds of prevalent HCV infection if inject stimulants compared to prevalent HCV infection if not inject stimulants	OR 2.43 (95%CI 1.33 – 4.43) for amphetamines	OR 2.92 (95%CI 2.50 – 3.40) for cocaine	OR 2.43 (95%CI 1.33 – 4.43) for amphetamines	Lognormal	**Table I1** of this manuscript, based on primary class of stimulant injected[24,67]
Proportion of HIV cases due to sexual transmission	17% (7% - 29%)	17% (7% - 29%)	14% (6% - 27%)	Beta	[68] [55] Estimates based on our previous coinfection modeling

PWID: people who inject drugs, HCV: hepatitis C virus, ART: antiretroviral therapy, IRR: incidence rate ratio, OR: odds ratio, PY: person-years

Table H4: Model input parameter values and distributions

Parameter	Mean sampled value (95%CI)	Sampling distribution	Reference
Average duration of injection until final cessation in years ($1/\mu_3$)	B: 11 (min=5, max,20) M: 11 (min=5, max,20) S: 11 (min=5, max, 30)	Triangular	[55,69] Increased upper bound for St. Petersburg due to evidence injecting duration may be longer.
Background drug-related mortality rate per year (μ_2)	2.35 per 100 PY (95%CI 0.0213-0.0257)	uniform (min= 0.0212 max= 0.0258)	[70]
Cofactor increase in HIV transmission during: Initial acute phase of high viremia compared to latent (ε)	14.5 (95%CI 3.6-25.4)	uniform (min=3, max=26)	[51,71]
Cofactor increase in HIV transmission during: pre-AIDS phase of high viremia compard to latent (ι)	4.0 (95%CI 1.2-6.9)	uniform (min=1, max=7)	[51,71]
Duration of initial period of high viremia in years ($1/\gamma$)	0.24		[51]
Duration of latent period of viremia in years ($1/\kappa$)	8.38		[51]
Duration of pre-AIDS period of high viremia in years ($1/\tau$)	0.75		[51]
Duration of AIDS period in years ($1/\theta$)	0.83		[51]
ART discontinuation rate per year (δ_c)	6.5% (95%CI 3.2%-9.8%)	uniform	[72,73]
Relative sexual-related transmissibility while on ART compared to latent phase (ω_{sex})	0.07 (95%CI 0.02-0.22)	lognormal	[74]
Relative injection-related transmissibility while on ART compared to latent phase (ω_{inj})	0.50 (95%CI 0.26-0.74)	uniform	[58] Uncertain, see webappendix text
Cofactor reduction in HIV mortality rate if initiating ART in latent or pre-AIDS stage (ν)	0.27 (95%CI 0.20-0.33)	uniform	[72]
Cofactor reduction in HIV mortality rate if initiating ART in AIDS stage (ρ)	0.51 (95%CI 0.39-0.62)	uniform	[75]
Relative HIV injection transmission risk if on NSP only compared to off NSP (RR_{NSPHIV})	0.42 (95%CI 0.22-0.81)	lognormal	[76]
Relative HCV injection transmission risk if on NSP compared to off NSP (RR_{NSPHCV})	0.79 (95%CI 0.39-1.61)	Lognormal	[77]
Factor increase in HCV transmissibility among HIV-infected not on ART (ϕ)	2.5 (95%CI 1.8-3.4)	Lognormal	[53]
Proportion HCV spontaneous clearance among HIV negative (ϵ)	26% (95%CI 22%-29%)	uniform	[52]
Proportion HCV spontaneous clearance among HIV positive (ϑ)	15% (95%CI 10%-20%)	uniform	[78,79]

HCV: hepatitis C virus, ART: antiretroviral therapy, PY: person-years, NSP: needle and syringe programs

Model analyses

For each scenario, we simulate the epidemic forward in time assuming no change in stimulant injection or intervention coverage. We estimated the proportion of incident HIV and HCV infections projected to occur over the next year among PWID who inject stimulants by dividing the expected number of incident cases among stimulant injectors by the number of all incident cases.

We additionally estimated the contribution of stimulant injection on incident HIV and HCV infection over the next year. To do this, we compare the total expected number of HIV and HCV infections in

our baseline epidemic to a counterfactual scenario where we assume no increased injecting or sexual risk associated with stimulant injection (e.g. relative risks set to 1).

Finally, we determined the impact of scaling-up an intervention such as high coverage NSP (receiving one or more sterile syringes for each injection) among PWID who inject stimulants on HCV and HIV incidence among stimulant injectors. High coverage NSP was assumed to reduce HIV and HCV transmission and acquisition based on data from systematic reviews.[77,80] We simulate a scale-up to 60% of PWID who inject stimulants receiving high coverage NSP, because this coverage level has been achieved in other global settings among PWID.[81] We calculated the overall percent decline in incidence over a 10-year intervention scale-up period.

Model calibration

Overall, model projections calibrated well to the data in all three illustrative scenarios, with 494, 483, and 492 accepted fits falling within the calibration data for the St-Petersburg-like, Montreal-like, and Bangkok-like scenarios, respectively. Calibration to the elevated odds of prevalent HCV among PWID who inject stimulants resulted in a roughly 3-fold simulated relative HCV incidence among PWID who inject stimulants compared to PWID who do not, regardless of stimulant class (2.9 [2.5-97.5% interval [95% interval, 95%I]: 1.9-4.5], 2.9 [95%I: 2.7–3.4], 2.8 [95%I: 2.0–4.1] in the St. Petersburg-like, Montreal-like and Bangkok-like scenarios, respectively). Calibration to steady-state HIV incidence data produced HIV prevalences among PWID of 36% (95%I: 27-42), 2.4% (95%I: 1.6-3.8), and 4.3% (95%I: 3.2–5.8) in the St. Petersburg-like, Montreal-like and Bangkok-like scenarios, respectively.

Sensitivity analyses

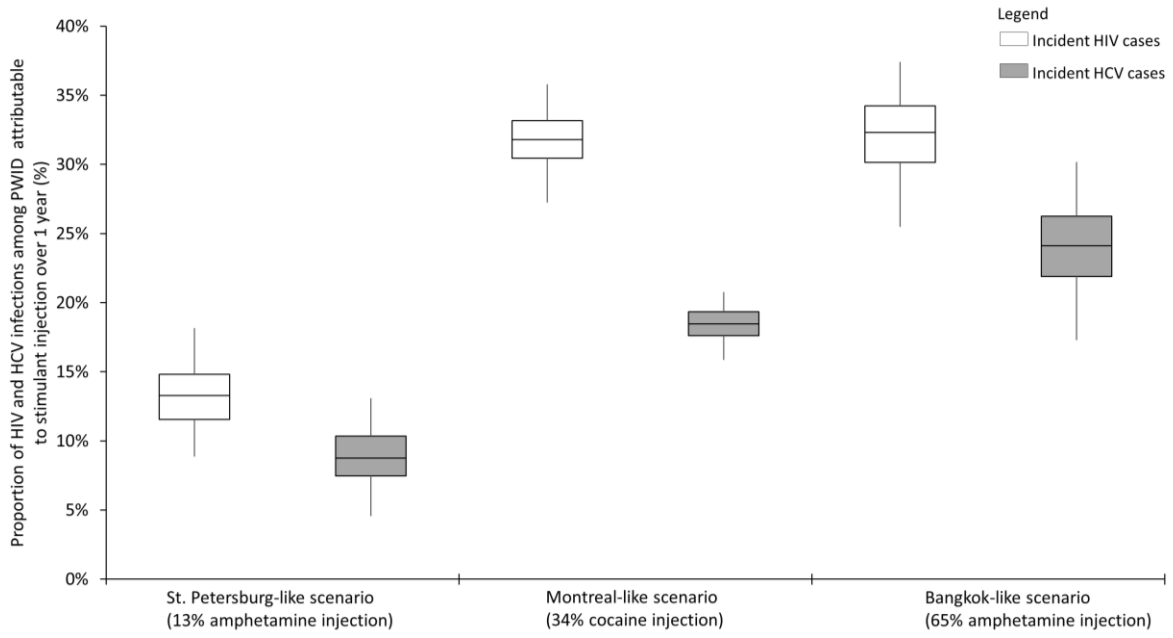
We conducted sensitivity analyses to assess robustness of modeling assumptions (**Figure H4**). First, we conducted a sensitivity analysis where we modeled 50% preferential (assortative) mixing by injecting risk (versus fully proportional). Preferential mixing resulted in minimal changes in the proportion of infections among PWID who inject stimulants in the next year (**Figure H4**). Compared to the base-case results, preferential mixing resulted in moderate reductions in the population attributable fraction of stimulant injection over 1 year. For example, in the St. Petersburg-like scenario, preferential mixing resulted in a mean HIV-related PAF of stimulant injecting of 11.3%, compared to the 14.8% with proportional mixing. In the Montreal-like scenario, preferential mixing resulted in a mean HIV-related PAF of stimulant injecting of 24.9%, compared to the 28.0% with proportional mixing. Finally, in the Bangkok-like scenario, preferential mixing resulted in a mean HIV-related PAF of stimulant injecting of 27.4%, compared to the 31.9% with proportional mixing.

Second, we conducted analyses examining the influence of turnover between PWID who inject stimulants and those who do not. Due to lack of data on this, we examined a scenario where PWID injected stimulants for an average duration of 5 years. We assumed all individuals entered into the non-stimulant compartments and were then recruited into stimulant injection, achieving the same level of coverage as in the base-case analyses. For this analysis, we calibrated to the IRR among PWID who inject stimulants for HIV from the systematic review (as in the base-case), and to the estimated IRR for HCV generated from the base-case calibration for each setting (because simulations calibrating to the OR for HCV generated unrealistic results, particularly in settings with high prevalence of stimulant use where differences in HCV *prevalence* by current stimulant injection could not be attained with high levels of turnover). Hence, our sensitivity analyses examined the impact of turnover with the same relative differences in HIV and HCV incidence between those who inject stimulant and those do not.

In the St. Petersburg-like scenario, we found that turnover resulted in a mean PAF of stimulant injecting of 15.3%, compared to 14.8% with no turnover. In the Montreal-like scenario, we found that turnover resulted in a mean PAF of stimulant injecting of 26.7%, compared to 28.0% with no turnover. In the Bangkok-like scenario, we found that turnover resulted in a mean PAF of stimulant injecting of 31.9%, compared to 31.6% with no turnover.

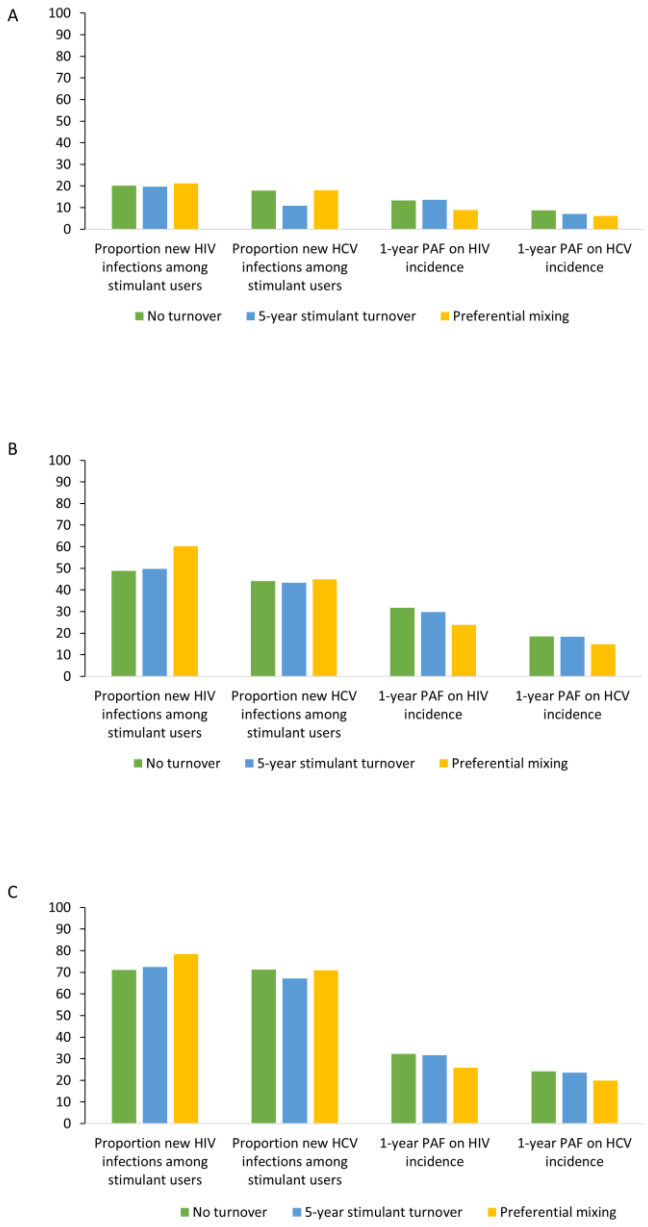
Third, we note that all scenarios examined had relatively high burden of HCV. As such, and given the heterogeneity in HCV prevalence across regions, we examine a sensitivity analysis assuming a lower prevalence of chronic HCV (25%) in our Bangkok-like scenario (compared to 75% at baseline). In this sensitivity analysis, stimulant injection is associated with a mean PAF of 27% for HCV in the next year, compared to 24% with a higher HCV prevalence at baseline. Per each 10% of the population using stimulants, in our sensitivity analysis this equates to a PAF of 4% for HCV, which is within the range found across our scenarios (3-7%).

Figure H3: Proportion of incident HIV (white boxes) and HCV (grey boxes) infections among PWID attributable to risks associated with stimulant injection over one year across three illustrative scenarios.



Line denotes the median, with boxes denoting the 25-75% centile range, and the whiskers denoting the 2.5-97.5% centile range.

Figure H4: Sensitivity analyses on the median proportion of new HIV and HCV infections among stimulant injectors and population attributable fraction in one year in St. Petersburg-like scenario (A), Montreal-like scenario (B), and Bangkok-like scenario (C).



Green, blue and orange bars denote the median proportions in the no turnover (base case), 5-year stimulant turnover, and preferential mixing scenarios, respectively.

Modelling HIV and suicide risk among MSM/TW who use stimulants in Lima, Peru

Prevalence of stimulant use is relatively high among men who have sex with men (MSM) and transgender women (TW) in a range of settings, including in Lima, Peru, where cocaine is the most commonly used stimulant. As stimulant use has been associated with higher risk sexual behaviours and higher risk of suicide among MSM/TW, we investigated the burden of both harms among MSM/TW in Lima using mathematical modelling. We modified a published mathematical model[82] of HIV transmission among MSM/TW in Lima to represent stimulant use and associated risks for HIV transmission and suicide mortality. We also used the model to investigate the impact of prioritizing HIV pre-exposure prophylaxis among MSM/TW who use stimulants versus random allocation by stimulant use. In this technical appendix, we describe (1) the technical specification of the deterministic, compartmental model of sexual HIV transmission and suicide among MSM/TW, (2) the parameter values and sources for Lima, Peru (3) the model fitting procedure.

Technical specification of the MSM/TW model

Full detail of the original model has been published,[82] but we provide an updated description of its specifications, including the representation of stimulant use and suicide mortality as well as updated data sources.

Definition of MSM/TW groups

To represent HIV spread in the model, we defined four interacting groups of MSM/TW: men who have sex with men and women (MSMW) and generally identify as heterosexual or bisexual, men who mostly have sex with men (MMSM) and generally identify as homosexual/gay, male sex workers, corresponding to men who reported having anal sex with men in exchange for money, drugs, gifts or favours in the past 12 months, and TW at higher risk, including those who engage in sex work. These categories are intended to represent a broad spectrum of gender identities, sexual orientations and risk contexts which are associated with sexual behaviours including numbers of partners, types of partnerships formed (stable, casual, commercial), condom use, and sexual positioning.

Stimulant use and HIV risk

A study using data from the Peruvian 2002-2003 HIV surveillance round among MSM/TW found a significant positive association between HIV infection and cocaine use before or during sex. The 2011 surveillance round among MSM/TW is the most recent source of comprehensive sexual behaviour data among MSM/TW in Peru, with a total sample of 5575 across all sites in Peru and

3182 in Lima. Using these 2011 data, associations between stimulant use (cocaine, cocaine paste, poppers, amphetamines) and sexual risk behaviours, including high number of partners, unprotected sex and sex work were found, suggesting HIV risk is higher among MSM/TW who use stimulants and that this has persisted through time. We used the Lima sample from 2011 to calculate prevalence of stimulant use in the past 3 months in each group and we estimated the pooled relative risk between stimulant use and unprotected anal sex with MSM/TW using log-binomial regression (**Table H5**).

Variables were defined as follows:

Stimulant use: having used poppers, ecstasy, cocaine, cocaine paste and/or amphetamines in the past 3 months

Unprotected sex: Unprotected receptive or insertive anal sex at last sex with a man or TW in the past 3 months

Table H5. Prevalence of stimulant use and associated risk of unprotected sex among MSM/TW in Lima, Peru in 2011

	Prevalence of stimulant use in past 3 months (95%CI)
Men who mostly have sex with men (MMSM) N=852	6.22% (4.6-7.8)
Men who mostly have sex with women (MMSW) N=593	13.32% (10.6-16.1)
Male sex workers (MSW) N=847	23.61% (20.7-26.5)
Transgender women (TW) N=449	17.82% (14.3-21.4)
	Association between stimulant use past 3 months and NO condom use
Relative risk of condom use at last sex with a man or transgender woman among MSM/TW who use stimulants versus not	RR 1.35 (95%CI 1.17-1.57) p<0.0001

We further disaggregated the population in the epidemic model in two groups by stimulant use in the past 3 months (yes/no) and incorporated the increased risk of unprotected sex among MSM/TW who use stimulants in the force of infection calculation (further detail and equations provided in section **Force of infection**).

Little is known about the average duration of stimulant use among MSM and TW, but studies indicate that use can be chronic with some individuals reporting use for over 20 years, while for others, use is sporadic over shorter periods of time. Given drug use is more common among the MSM/TW communities and that the populations represented here, and particularly MSW and TW, experience a range of social vulnerabilities, we assumed stimulant use to be constant while sexually active with other MSM/TW. A fixed proportion in each group were therefore assumed to use stimulants at entry into the model and remained in this state until they exited the population. We

performed a sensitivity analysis assuming an average duration of stimulant use of 5 years in order to investigate the impact of this assumption on our model findings.

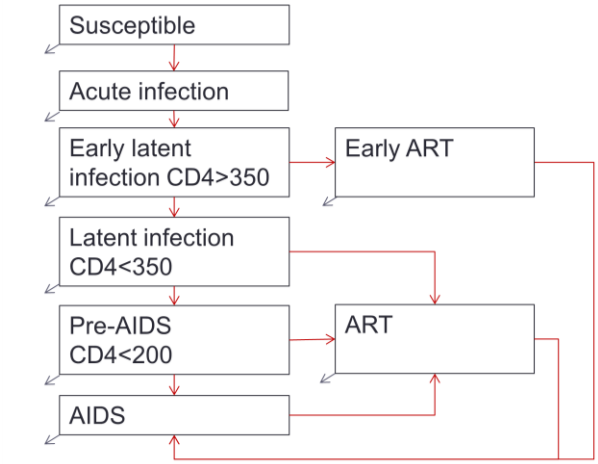
Stimulant use and suicide

While high rates of suicidal ideation and attempt among MSM/TW have been reported in Peru, estimates of suicide mortality among MSM/TW are not available (and these are difficult to obtain across settings). We therefore applied the crude mortality rate (CMR) associated to suicide among people who use stimulants obtained from the literature review (0.07/100 person years (0.04, 0.10), Table 1 in the main text) to all MSM/TW. Among MSM/TW who do not use stimulants, we divided it by the standard mortality ratio (SMR) for the increased risk of suicide among people who use stimulants, also obtained from the literature review (6.26 (2.84, 13.80), Table 1 in the main text). To represent uncertainty in these values, we sampled from the 95% confidence interval of the CMR and the SMR using the lognormal distribution.

HIV progression and treatment

The course of HIV infection was represented as distinct phases of disease progression defined by duration and infectiousness (**Figure H5**)[83]. When an individual gets infected, they enter a phase of acute infection (short duration, high infectiousness) and progresses to a latent phase with a CD4 cell count >350 cells/mm^3 and to a latent phase with a CD4 cell count<350-200 cells/mm^3 (both have long duration, low infectiousness), before entering a pre-AIDS phase with a CD4 cell count<200 cells/mm^3 (short duration, high infectiousness). The disease finally progresses to an AIDS phase (short duration, no infectiousness due to an interruption of sexual activity), followed by death. HIV positive individuals receive antiretroviral treatment (ART) during the latent or pre-AIDS stage at a rate that varies by stage. ART reduces infectiousness and extends survival. The earlier the initiation of ART, the longer the increase in life expectancy.

Figure H5 – Progression of HIV infection in MSM/TW model



MSM/TW initially enter the model as susceptible and spend an average time period in the population, corresponding to the average duration of their sexual activity with MSM/TW. Homosexual and bisexual men have a slower turnover than TW at higher risk and male sex workers, which reflects the lower life expectancy among TW and the transitional aspect of sex work. Once individuals exit the model, they are replaced and allocated to each group according to the initial population distribution by group. The population grows at an average rate of 2%.[84] Condom use was modelled to increase linearly from 1995 until 2005, and to remain constant at the rate reported thereafter.[85] ART was introduced free of charge in Peru in 2004.[86] To account for the fact that ART started being provided to some people before this policy change, we modelled its introduction with a small coverage starting in 2002 and a linear increase up to reach a coverage of 80% of HIV positive individuals with <200 CD4 cells/mm^3 (preAIDS stage) in 2007.[87] In 2012 national guidelines changed recommending treatment to HIV positive individuals with 200-350 CD4 cells/mm^3. Guidelines changed again in December 2015 to include patients with a CD4 count <500 cells/mm^3 and treatment independent of CD4 count was adopted in Peru in March 2018. We modelled a slow linear increase in coverage among those in the (late) latent infection, pre-AIDS and AIDS stages between 2002 and 2012 and fitted treatment rates to the estimated coverage among MSM/TW in 2011.[88] We modelled a faster increase from 2012 to reflect the expansion of treatment guidelines and introduced treatment among those in early latent infection in 2016 to reflect the expansion of treatment guidelines in 2016 and 2018. These changes in guidelines have not resulted in a substantial increase in ART treatment access among MSM/TW, but we assumed coverage would keep increasing in the future at a constant rate.

Model equations

The model is defined by ordinary differential equations to simulate how HIV spreads over time. They are shown below. The state variables are given by $X^{s}_{k,f,a}(t)$ and $XP^{s}_{k,f,a}(t)$, corresponding to people who are not on PrEP and to people either on PrEP (while susceptible) or who have been on PrEP (if infected), respectively. *t* is the time elapsed in the simulation; *s* is the infection-status (1= susceptible; 2= acute infection; 3= latent infection; 4= pre-AIDS; 5= AIDS; 6= ART; 7=late ART), *k* is 'sexual behaviour' (1= Insertive MSMW; 2=Versatile MSMW; 3=Insertive MMSM; 4=Versatile MMSM; 5=Receptive MMSM; 6=Insertive sex worker; 7=Versatile sex worker; 8=Receptive sex worker; 9= receptive TW at a higher risk), f is 'stimulant use' (1=no; 2=yes), *a* is the PrEP adherence group (1=good; 2=average; 3=poor).

$$\frac{dX^{1}_{k,f}(t)}{dt} = \gamma_{k,a,f}\left\{(\mu+\alpha(t))\sum_{k,f,a}^{s}\left(X^{s}_{k}+XP^{s}_{k,f,a}\right)+\sigma_5\sum_{k,f,a}\left(X^{5}_{k,f}+XP^{5}_{k,f,a}\right)+\sum_{k}\left(\tau_k\sum_{a,f}^{s}\left(X^{s}_{k,f}+XP^{s}_{k,f,a}\right)\right)+\sum_{f}\left(\varpi_f\sum_{k,a}^{s}\left(X^{s}_{k,f}+XP^{s}_{k,f,a}\right)\right)\right\}$$
$$-\lambda_{k,f}X^{1}_{k,f}-(\mu+\tau_k+\varpi_f)X^{1}_{k,f}$$

$$\frac{dX^{2}_{k,f}(t)}{dt} = \lambda_{k,f}X^{1}_{k,f}-\left(\sigma_2+\mu+\tau_k+\varpi_f\right)X^{2}_{k,f}$$

$$\frac{dX^{3}_{k,f}(t)}{dt} = \sigma_2X^{2}_{k,f}-\left(\sigma_3+\delta(t)+\mu+\tau_k+\varpi_f\right)X^{3}_{k,f}$$

$$\frac{dX^{4}_{k,f}(t)}{dt} = \sigma_3X^{3}_{k,f}-\left(\sigma_4+\vartheta(t)+\mu+\tau_k+\varpi_f\right)X^{4}_{k,f}$$

$$\frac{dX^{5}_{k,f}(t)}{dt} = \sigma_4X^{4}_{k,f}+\sigma_6X^{6}_{k,f}+\sigma_7X^{7}_{k,f}-\left(\sigma_5+\mu+\tau_k+\varpi_f\right)X^{5}_{k,f}$$

$$\frac{dX^{6}_{k}(t)}{dt} = \delta(t)X^{3}_{k,f}-\left(\sigma_6+\mu+\tau_k+\varpi_f\right)X^{6}_{k,f}$$

$$\frac{dX^{7}_{k}(t)}{dt} = \vartheta(t)X^{4}_{k,f}-\left(\sigma_7+\mu+\tau_k+\varpi_f\right)X^{7}_{k,f}$$

Susceptible on PrEP and infected while they were on PrEP:

$$\frac{dXP^{1}_{k,f,a}(t)}{dt} = -\lambda P_{k,a,f}XP^{1}_{k,f,a}-(\mu+\tau_k+\varpi_f)XP^{1}_{k,f,a}$$

$$\frac{dXP^{2}_{k,f,a}(t)}{dt} = \lambda_{k,a,f}XP^{1}_{k,f,a}-\left(\sigma_2+\mu+\tau_k+\varpi_f\right)XP^{2}_{k,f,a}$$

$$\frac{dXP^{3}_{k,f,a}(t)}{dt} = \sigma_2XP^{2}_{k,f,a}-\left(\sigma_3+\delta(t)+\mu+\tau_k+\varpi_f\right)XP^{3}_{k,f,a}$$

$$\frac{dXP^{4}_{k,f,a}(t)}{dt} = \sigma_3XP^{3}_{k,f,a}-\left(\sigma_4+\vartheta(t)+\mu+\tau_k+\varpi_f\right)XP^{4}_{k,f,a}$$

$$\frac{dXP^{5}_{k,f,a}(t)}{dt} = \sigma_4XP^{4}_{k,f,a}+\sigma_6XP^{6}_{k,f,a}-\left(\sigma_5+\mu+\tau_k+\varpi_f\right)XP^{5}_{k,f,a}$$

$$\frac{dXP^{6}_{k,f,a}(t)}{dt} = \delta(t)XP^{3}_{k,f,a}-\left(\sigma_6+\mu+\tau_k+\varpi_f\right)XP^{6}_{k,f,a}$$

$$\frac{dXP^{7}_{k,f,a}(t)}{dt} = \vartheta(t)XP^{4}_{k,f,a}-\left(\sigma_7+\mu+\tau_k+\varpi_f\right)XP^{7}_{k,f,a}$$

Flow to PrEP

$$X^1_{k,f} \rightarrow X^1_{k,f} - V_{k,f}(t)\sum_a \left(X^1_{k,f} + XP^1_{k,f,a}\right) - \sum_a XP^1_{k,f,a}$$

$$XP^1_{k,f,a} \rightarrow XP^1_{k,f,a} + u_a\left(V_k(t)\sum_a \left(X^1_{k,f} + XP^1_{k,f,a}\right) - \sum_a XP^1_{k,f,a}\right)$$

$1/\sigma_s$ is the mean time spent in infection phase *s*; $\lambda_{k,f}$ and $\lambda_{k,a,f}$ correspond to the force of infection for individuals in each group, depending on their sexual identity/practices, stimulant use and PrEP adherence if on PrEP; μ is the death rate, ϖ_f is the rate of suicide by stimulant use, $\frac{1}{\tau_k}$ is the net mean time spent in each sexual behaviour group. $\alpha(t)$ is the population growth rate over time; $\gamma_{k,a,f}$ is the proportion of people by sexual behaviour, PrEP adherence and stimulant use. A certain proportion of infected individuals receive early ($\delta(t)$) or late ($\vartheta(t)$) ART depending on coverage at time t. People who exited the population due to background death, suicide, AIDS related death or population turnover are continuously replaced into the susceptible group X^1 and distributed according to $\gamma_{k,a,f}$. Equally, susceptible individuals who are not on PrEP continuously move to the "susceptible on PrEP" compartment ($XP^1_{k,f,a}(t)$) so that the PrEP coverage at that time point $V_{k,f}(t)$ is maintained. They are distributed into each adherence group according to υ_a.

PrEP allocation by stimulant use

We investigated two scenarios to compare the effectiveness of prioritizing PrEP to all MSM/TW who use stimulants versus allocating PrEP independently of stimulant use in each of these groups (called "random allocation" hereafter). In the first scenario we simulated 100% PrEP coverage among HIV susceptible MSM/TW who use stimulants, varying between approximately 6% and 24% depending on the group and 0% coverage among MSM/TW who do not use stimulants. In the second scenario, the same proportion of each group is covered by PrEP, reproducing PrEP coverage per group in the prioritization scenario, but it is allocated proportionally among MSM/TW who use stimulants and those who do not. These two scenarios allow us to evaluate the relative effectiveness of PrEP prioritization to MSM/TW who use stimulants.

Scenario 1 (PrEP prioritization by stimulant use): $\varsigma_{k,2}(t) = 1$, $\varsigma_{k,1}(t) = 0$

Scenario 2 (Random PrEP allocation): $\varsigma_{k,f}(t) = \frac{X^1_{k,2}}{\sum_f X^1_{k,f}}$ as obtained from scenario 1. In this way, the proportion receiving PrEP in each group is the same as in scenario 1, but the allocation is done randomly in regards to stimulant use.

The boundary conditions of the system are:

$$X^{1}_{k,a,f}(0) = (1 - seed)\gamma_{k,a,f} N_0$$

$$X^{3}_{k,a,f}(0) = (seed)\gamma_{k,a,f} N_0$$

N_0 is the size of the MSM and TW population at the start of the simulation and $seed$ is the HIV prevalence at the start of the simulation in all parts of the population.

Force of infection

The force of infection determines the rate of progression from susceptible to infected. The force of infection through sexual contact depends on: the number of insertive and receptive partnerships C^i and C^r, respectively, the pattern of sexual partnership formation with respect to sexual behaviour (i.e. the proportion of partnerships formed with each of the sexual behaviour groups for insertive and receptive partnerships ($\rho^{i}_{k,k',f,f'}$ and $\rho^{r}_{k,k',f,f'}$ respectively by stimulant use status), the number of sex acts occurring within that partnership ($\omega_{k,k'}$), the infection-status and stage of infection of the partner, the fraction of sex acts in which a condom is used by sexual behaviour group and stimulant status ($\phi_{k,k',f,f'}$) and the efficacy of condoms in reducing the risk of HIV transmission (ψ). β^{i}_{s} and β^{r}_{s} are the probabilities of HIV transmission per sex act for each stage of infection for insertive and receptive anal sex respectively. For individuals using PrEP, it will also depend on their adherence to the PrEP regimen, which determines the proportion of sex acts protected by PrEP (η_a) and on the efficacy of PrEP (θ). Functional PrEP effectiveness (based on adherence patterns and efficacy) was assumed to be 80% based on the PROUD[89] and Ipergay[90] trials, although it may be lower in Peru and among specific populations such as TW. This simplification was made to increase generalizability of our findings in the context of the review.

The frequency of condom use in partnerships is specific to each sexual behaviour group and is determined by the receptive partner. The increased risk of unprotected sex among those using stimulants was implemented through a relative risk. In partnerships in which either one or both of the partners used stimulants, condom use was reduced by the corresponding relative risk.

Off PrEP

$$\lambda_{k,f} = \sum_{k',f'} C_k^i \rho_{k,k',f,f'}^i \left[\frac{\sum_{s=2}^{7} (X_{k',f'}^s + \sum_a XP_{k',a,f'}^s)}{\sum_s \left(X_{k',f'}^s + \sum_a XP_{k',a,f'}^s \right)} \left(1 - \left(\left(1 - \beta_s^i \right)^{\omega_{k,k'}(1-\phi_{k,k',f,f'})} \left(1 - \beta_s^i \psi \right)^{\omega_{k,k'}\phi_{k,k',f,f'}} \right) \right) \right]$$

$$+ \sum_{k',f'} C_k^r \rho_{k,k',f,f'}^r \left[\frac{\sum_{s=2}^{7} (X_{k',f'}^s + \sum_a XP_{k',a,f'}^s)}{\sum_s \left(X_{k',f'}^s + \sum_a XP_{k',a,f'}^s \right)} \left(1 - \left(\left(1 - \beta_s^r \right)^{\omega_{k,k'}(1-\phi_{k,k',f,f'})} \left(1 - \beta_s^r \xi_{k,k'} \psi \right)^{\omega_{k,k'}\phi_{k,k',f,f'}} \right) \right) \right]$$

On PrEP

$$\lambda_{k,a,f} = \sum_{k',f'} C_k^i \rho_{k,k',f,f'}^i \left[\frac{\sum_{s=2}^{8} (X_{k',f'}^s + \sum_a XP_{k',a,f'}^s)}{\sum_s \left(X_{k',f'}^s + \sum_a XP_{k',a,f'}^s \right)} \left(1 - \left(\begin{array}{l} \left(1 - \beta_s^i \right)^{\omega_{k,k'}(1-\phi_{k,k',f,f'})(1-\eta_a)} \left(1 - \beta_s^i \psi \right)^{\omega_{k,k'}\phi_{k,k',f,f'}(1-\eta_a)} \\ \left(1 - \beta_s^i \theta \right)^{\omega_{k,k'}(1-\phi_{k,k',f,f'})\eta_a} \left(1 - \beta_s^i \psi \theta \right)^{\omega_{k,k'}\phi_{k,k',f,f'}\eta_a} \end{array} \right) \right) \right]$$

$$+ \sum_{k',f'} C_k^r \rho_{k,k',f,f'}^r \left[\frac{\sum_{s=2}^{8} (X_{k',f'}^s + \sum_a XP_{k',a,f'}^s)}{\sum_s \left(X_{k',f'}^s + \sum_a XP_{k',a,f'}^s \right)} \left(1 - \left(\begin{array}{l} \left(1 - \beta_s^r \right)^{\omega_{k,k'}(1-\phi_{k,k',f,f'})(1-\eta_a)} \left(1 - \beta_s^r \psi \right)^{\omega_{k,k'}\phi_{k,k',f,f'}(1-\eta_a)} \\ \left(1 - \beta_s^r \theta \right)^{\omega_{k,k'}(1-\phi_{k,k',f,f'})\eta_a} \left(1 - \beta_s^r \psi \theta \right)^{\omega_{k,k'}\phi_{k,k',f,f'}\eta_a} \end{array} \right) \right) \right]$$

Mixing matrix

The mixing matrix designs the proportion of partnerships that are formed with individuals from each of the groups. The first step is to determine who has sex with whom. Since our groups are divided in insertive, receptive and versatile roles, there are certain combinations that cannot occur: two insertive individuals. To balance the number of insertive and receptive partnerships we first defined a mixing matrix for the insertive individuals, reflecting their preference for certain types of partners, as well as a random mixing matrix where insertive individuals chose their partner according to the proportion of sex acts offered by each of the receptive groups - this assumes that the amount of sex the "providers" have is totally dependent of the demand. The extent to which the mixing was closer to satisfy the preferences of insertive individuals was determined by a parameter ε varying from one (totally assortative mixing) to zero (totally random mixing). The total number of partners among the receptive groups was then recalculated to respond to the demand and the mixing matrix for receptive individuals was updated.

$$\rho_{k,k'}^i = \left(\varepsilon A_{k,k'} + (1-\varepsilon) B_{k,k'} \right)$$

$$B_{k,k'} = \frac{C_{k'}^r \left(\sum_s X_{k',1}^s + \sum_{a,s} X_{k',a}^s \right)}{\sum_{k'} C_{k'}^r \left(\sum_s X_{k',1}^s + \sum_{a,s} X_{k',a}^s \right)}$$

$$C_k^r{}' = \frac{C_{k'}^i \rho_{k',k}^i \left(\sum_s X_{k'}^s + \sum_{a,s} X_{k',a}^s \right)}{\sum_s X_k^s + \sum_{a,s} X_{k,a}^s}$$

$$\rho^{r}_{k,k'} = \frac{C^{i}_{k'}\rho^{i}_{k',k}\left(\sum_{s} X^{s}_{k'} + \sum_{a,s} X^{s}_{k',a}\right)}{C^{r}_{k}{}'\left(\sum_{s} X^{s}_{k} + \sum_{a,s} X^{s}_{k,a}\right)}$$

$$\rho^{i}_{k,k',f,f'} = \rho^{i}_{k,k'}\theta_{f'}$$

$$\rho^{r}_{k,k',f,f'} = \rho^{r}_{k,k'}\theta_{f'}$$

$\rho^{i}_{k,k'}$ and $\rho^{r}_{k,k'}$ define the proportion of total partnerships in group k that are formed with group k' for insertive and receptive partnerships respectively. $A_{k,k'}$ is the expected proportion of partnerships that insertive individuals in group k will have with receptive individuals in group k' and $B_{k,k'}$ is the proportion of receptive partnerships given by receptive individuals in group k' out of the total number of partnerships C^{r} given by all receptive individuals in all groups. ε determines the extent to which the mixing is in accordance to the insertive partners preferences or dependent on availability. $C^{r}_{k}{}'$ is the updated number of receptive partnerships individuals in group k give in order to respond to the demand. $\rho^{i}_{k,k',f,f'}$ and $\rho^{r}_{k,k',f,f'}$ define the proportion of total partnerships in group k and f that are formed with group k' and f', for insertive and receptive partnerships respectively. It assumes that mixing in function of stimulant use occurs randomly (i.e. the proportion of partnerships occurring with MSM/TW who use stimulants is equal to the proportion of MSM/TW who use stimulants).

Model parameterisation: values and sources

Demography

Parameters that describe the basic demography of the population are provided in **Table H6.**

Table H6 – Basic demography of the population

Parameters	Description	Value	Reference
Population 15 to 49y	2007	4,767,148	[84]
Population 15 to 49y	1981	2,503,140	[91]
First report of AIDS cases in Peru		1983	[92]
Proportion of the population that are men in Lima, Peru	2007	0·489	[84]
Proportion of male-to-male sex in general population		0·06	[93-95]

HIV progression and treatment

Parameters that define the natural history of HIV (**Table H7**) were estimated from the global scientific literature. For reasons of computational efficiency, the uncertainty in these parameter values is not reflected in the estimates of uncertainty, with the exception of β^{3-4} which corresponds to the baseline HIV transmission probability during an insertive anal sex act in the latent phase of infection.

Table H7 – Natural history of HIV model parameters

Parameters	Description	Symbol	Prior Value mode [min-max]	Prior Value mean[variance]	Posterior Value mean[variance]	Reference
Average transmission rate of HIV per sex act	if latent HIV infection	β^{3-4}	0·0028[0·002-0·004]	0.0026[3.8 10-7]	0.0029[1.5x10^{-7}]	96
Start of the epidemic	year		[1970-1982]	1976[12]	1972[6.9]	92
Relative transmission rate per insertive anal sex act			1			Def.
Relative transmission rate per receptive anal sex act	(ref. insertive anal sex)	ξ	5			97,98
Relative infectiousness in acute phase infection	(ref. latent infection)	β^{2}	27			83
Relative infectiousness in latent phase infection		β^{3-4}	1			Def.
Relative infectiousness in pre-AIDS phase infection	(ref. latent infection)	β^{5}	7·2			83
Relative infectiousness in AIDS phase infection	(ref. latent infection)	β^{6}	0			83
Relative infectiousness of virally-suppressed individuals on ART	(ref. latent infection)	β^{7-8}	0·2			83,99
Mean duration of acute phase infection	months	$1/\sigma_2$	3			83,99
Mean duration of latent phase	years	$1/\sigma_3$	10			83,99
Mean interval with elevated viral load, pre-AIDS	months	$1/\sigma_4$	10			83,99
Mean interval with AIDS before death	months	$1/\sigma_5$	9			83,99
Mean duration on ART among those starting early (latent)	years	$1/\sigma_6$	25			
Mean duration on ART among those starting late (pre-AIDS)	years	$1/\sigma_7$	12			
Mean ART initiation rate among those in latent, pre-AIDS, AIDS	2002-2012 (slow) 2012-2030 (faster)	*ART_covlate*	0.05-0·15		0.10[8.6x10^{-4}]	87,88,100
Mean ART initiation rate among those in the early latent stage	2016-2030	*ART_cov*	0.05-0.15		0.10 [9.5x10^{-4}]	Assumption
Efficacy of condoms		ψ	0.7			101,102

Table H8 – Distribution of risk in the population and risk behaviours

Parameter	Prior Value Mode [min-max]	Prior Value Mean [variance]	Posterior Value Mean [variance]	Reference
Proportion of all MSM/TW: MSMW	0·2 [0·08-0·3]	0.19[0.002]	0.18 [0.002]	85,93,103-105
Proportion of all MSM/TW: sex worker	0·15 [0·1-0·25]	0.17[0.001]	0.18 [0.001]	85,103,105-108
Proportion of all MSM/TW: Transwomen	0·05 [0·04-0·07]	0.06[0.0002]	0.05[0.0001]	103
Mean duration: MSMW	20-40	27 [8.3]	27 [8.0]	Assumption
Mean duration: MMSM	20-40	27[8.3]	26[8.1]	Assumption
Mean duration: sex worker	2-20	4[5]	5[4.5]	Assumption
Mean duration: Transwomen	10-30	15[8.3]	15[7.6]	Assumption
N sex acts per commercial partnership	1-2	1.5[0.08]	1.7[0.05]	Assumption
N sex acts per stable partnership	20-50	35[57]	29 [50]	109
N sex acts per casual partnership	3-15	9[12]	8 [9]	110
Condom change	2.5-3.5	3[0.02]	3.1[0.07]	85,103,111,112
Epsi (mixing matrix)	0.6[0.4-0.99]	0-66[0.015]	0.64[0.013]	Assumption
Sexual behaviour: MSMW				
Pr of all MSMW: insertive	0·85 [0·8-0·9]	0.85[0.0004]	0.85[0.0005]	113
N partnerships/year: MSMW insertive	2[1-4]	2.3[0.39]	2.0[0.42]	111,114
Pr of protected sex acts: MSMW insertive	0·10-0·17	0.13[0.0002]	0.13[0.0004]	110,113,114
N partnerships/year: MSMW versatile	3·5 [1.5-4]	3[0.29]	3 [0.29]	110,111,113,114
Pr of protected sex acts: MSMW versatile	0·10-0·17	0.13[0.002]	0.14[0.0004]	110,114
Sexual behaviour: MMSM				
Pr of all MMSM: insertive	0·25 [0·25-0·35]	0.25[0.0004]	0.25[0.0005]	104,108
N partnerships/year: MMSM insertive	1·2 [1-3]	1.7[0.20]	1.4[0.08]	111,115
Pr of protected sex acts: MMSM insertive	0·10-0·17	0.13[0.002]	0.135[0.0004]	114
Pr of all MMSM: receptive	0·325 [0·3-0·35]	0.33[0.0001]	0.32[0.0001]	104,108
N partnerships/year: MMSM receptive	3[1-4]	2.7[0.4]	2.6[0.35]	111,114
Pr of protected sex acts: MMSM receptive	0·10-0·18	0.15[0.002]	0.15[0.0004]	114
N partnerships/year: MMSM versatile	3.5 [1.5-4]	3[0.29]	2.9[0.35]	111,114
Pr of protected sex acts: MMSM versatile	0·10-0·18	0.15[0.002]	0.15[0.0003]	114
Sexual behaviour: sex worker				
Pr of all sex worker: insertive	0·20 [0·20-0·30]	0.2[0.0004]	0.2[0.0004]	115
N partnerships/year: sex worker insertive	30 [10-35]	25[29]	27[21]	115
Pr of protected sex acts: sex worker insertive	0·10-0·17	0.13[0.002]	0.13[0.0004]	115
Pr of all sex worker: receptive	0·4 [0·35-0·5]	0.42[0.001]	0.42[0.001]	115
N partnerships/year: sex worker receptive	30 [10-50]	30[67]	29[23]	115
Pr of protected sex acts: sex worker receptive	0·10-0·17	0.13[0.001]	0.13[0.0004]	115
N partnerships/year: sex worker versatile	50 [35-60]	48[39]	50[64]	115
Pr of protected sex acts: sex worker versatile	0·1-0·25	0.13[0.002]	0.13[0.0003]	115
Sexual behaviour: transgender women				
N partnerships/year: transgender women	80 [60-150]	97[439]	97[395]	110,111
Pr of protected sex acts: transgender women	0·10-0·16	0.13[0.001]	0.39[0.0003]	114

N: number; Pr: proportion; min: minimum; max: maximum; ref: reference.

Contribution of MSM/TW who use stimulants to HIV and suicide incidence

To estimate the excess burden of HIV incidence among MSM/TW who use stimulants we calculated the proportion of new HIV infections that are estimated to occur among this group in the next year (between 2020 and 2021) and calculated the excess incidence burden among this group by dividing the proportion of new infections in this group by the proportion of the total MSM/TW population who use stimulants.

Similarly, to estimate the excess burden of suicide incidence among MSM/TW who use stimulants we calculated the proportion of suicides that are estimated to occur among this group in the next year (between 2020 and 2021) and divided it by the proportion of the total MSM/TW population who use stimulants.

Model fit: methods and data

The epidemic was simulated with 10,000 different parameter sets randomly sampled through Latin hypercube sampling. The log likelihood of each epidemic trajectory was calculated based in time series HIV prevalence data for the total MSM/TW population and for each group (**Table H9**), time series HIV incidence data for the total MSM/TW population (**Table H10**), the proportion using stimulants per group in 2011 (**Table H5**) and the total ART coverage for 2011 based on Chow et al.[88] The fits with a log likelihood above the 99th percentile were selected for the analysis.

The parameters allowed to vary were those describing sexual behaviour as well as a couple describing the natural history of infection. Descriptive statistics for their prior and posterior distributions are given in **Tables H7** and **H8** when applicable. The parameters for which the posterior distributions diverged the most from the prior distribution were the basic transmission probability (towards higher values) and the year at which the epidemic started (towards earlier start) as well as the sex workers turnover (towards slower), the number of sex acts in a commercial partnership (towards higher values) and the number of sex acts in a stable partnership (towards lower values). In general, the selection process favoured parameter values that increased risk among sex workers and transwomen and decreased risk among MMSW.

Table H9. HIV prevalence by group in Lima, Peru

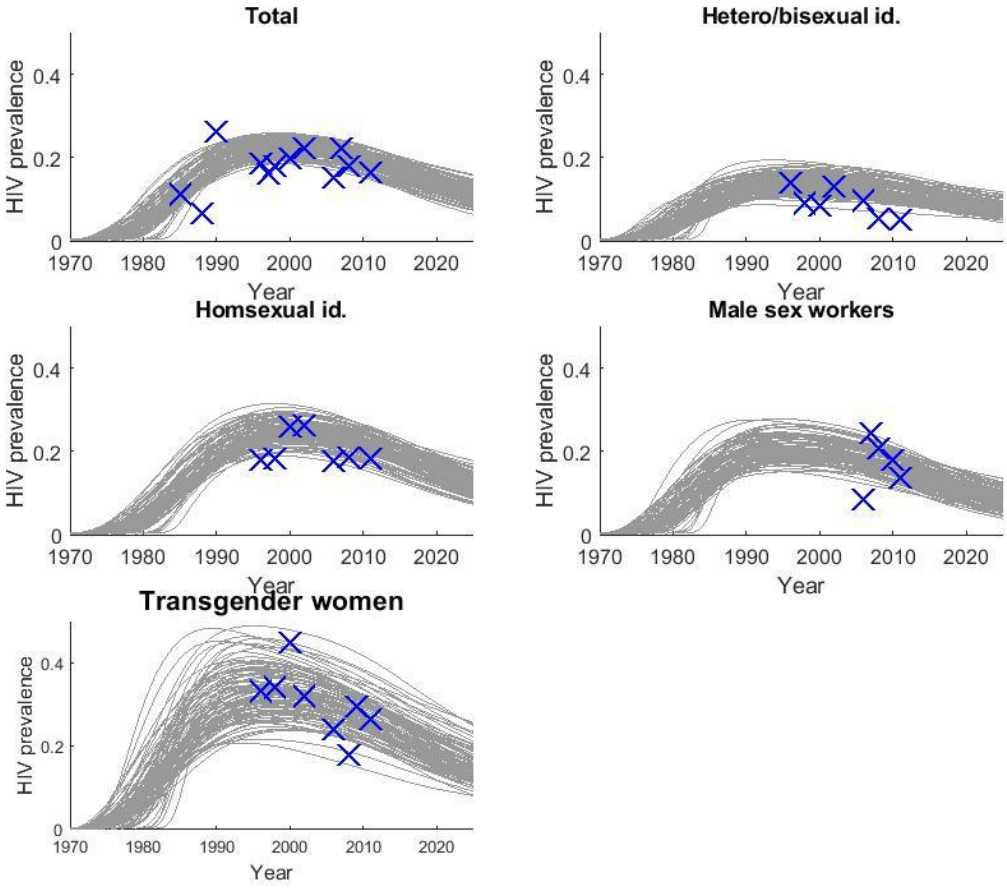
Population	Year	Sample size	Prevalence	Reference
All MSM/TW	1985	98	0·112	[116]
All MSM/TW	1988	124	0·065	[117]
All MSM/TW	1990	4300	0·262	[118]
All MSM/TW	1996	444	0·185	[85]
All MSM/TW	1997	1328	0·16	[119]
All MSM/TW	1998	1211	0·178	[85]
All MSM/TW	2000	1357	0·197	[85]
All MSM/TW	2002	1358	0·223	[85]
All MSM/TW	2006*	618	0.151	
All MSM/TW	2007	559	0·222	[108]
All MSM/TW	2008	318	0·179	[111]
All MSM/TW	2011*	2171	0.163	[120]
MSMW	1996	129	0·139	[85,114]
MSMW	1998	263	0·091	[85]
MSMW	2000	533	0·084	[85]
MSMW	2002	511	0·129	[85]
MSMW	2006*	185	0.097	
MSMW	2008	109	0·055	[121]
MSMW	2008	21	0·29	[111]
MSMW	2011*	283	0.05	[120]
MMSM	1996	265	0·18	[85,114]
MMSM	1998	796	0·181	[85]
MMSM	2000	661	0·26	[85]
MMSM	2002	562	0·262	[85]
MMSM	2006*	261	0.177	
MMSM	2008	253	0·186	[111]
MMSM	2011*	761	0.183	[120]
Transgender women	1996	48	0·333	[85,114]
Transgender women	1998	134	0·343	[85]
Transgender women	2000	96	0·448	[85]
Transgender women	2002	255	0·322	[85]
Transgender women	2006*	95	0.242	
Transgender women	2008	208	0·178	[111]
Transgender women	2009	459	0·296	[112]
Transgender women	2011*	368	0.264	[120]
Male sex workers	2006*	77	0.083	
Male sex workers	2007	169	0·243	[121]
Male sex workers	2008	391	0·207	[111]
Male sex workers	2011*	759	0.135	[120]

*The eligibility criteria for the 2006 and 2011 sentinel surveillance rounds excluded HIV positive MSM/TW who were aware of their status. We corrected these estimates based on the proportion of HIV positive MSM/TW who knew their status in a study preceding the 2011 round.

Table H10. HIV incidence (infections/100 person years)

Year	Incidence	Reference
1999	3·5 [2.3-4.7]	ALASKA cohort[105]
2002.5	5.3 [1.64-9.05]	BED, 8 neighbourhoods[122]
2006	3.2 [1.0-5.35]	BED sentinel surveillance[121,123]
2011	3.6	Comunidades positivas cohort[121,124]
2014	0.9	SABES cohort[121,125]

Figure H6 – Fits against prevalence data for four sub-groups and the overall MSM/TW population.



Baseline results

The model estimated that 1,225 (95% percentile: 667-1823) new HIV infections will occur among MSM and TW in Lima in the next year (between 2020 and 2021) and that 11.1% (9.7-13.3) will occur among MSM/TW who use stimulants. It estimated that 16 suicide deaths will occur among this population over the same year and that 39.1% (17.6-60.0) will be among MSM/TW who use stimulants.

Covering all susceptible MSM/TW who use stimulants with PrEP between 2020-2030 would avert 17.9% (9.1-34.9) of new HIV infections, while covering the same proportion of susceptible individuals in each group, but randomly allocating to MSM/TW who use and do not use stimulants would prevent 14.9% (7.4-30.2) of new

infections. This results in a relative effectiveness of the prioritization by stimulant use strategy of 19% (11-31) more new infections averted.

Alternative scenario

We also investigated a third extreme scenario is which the total PrEP coverage would be the same as in the scenarios above but with allocation being completely proportional across groups (independently of sexual identity/behaviors or stimulant use).

$$\varsigma_{k,f}(t) = \frac{\sum_{k} X^{1}_{k,2}}{\sum_{k,f} X^{1}_{k,f}}$$

This resulted in approximately 10% PrEP coverage in each group, proportionately distributed among MSM/TW who use and do not use stimulants. The proportion of new infections averted in this scenario was 12.2% (6.5-23.3) translating in a relative effectiveness of 45%(20-71) compared to the full prioritization among MSM/TW who use stimulants. This highlights the association between prevalence of stimulant use and HIV risk behaviours, suggesting prioritization by stimulant use might also translate in prioritization by a range of other risk factors, although this will be context specific. A comparison of the three scenarios illustrates the incremental effectiveness of prioritizing PrEP by risk and by stimulant use.

Sensitivity analyses

Duration of stimulant use. We implemented a sensitivity analysis to investigate the impact of assumptions about the duration of stimulant use. In our main analysis we assumed a lifetime duration of cocaine use, with a constant proportion of MSM/TW entering the model engaging in stimulant use. In our sensitivity analysis, we assumed the same constant proportion of MSM/TW using stimulants entering the model, but assumed an average duration of stimulant use of 5 years. The progression rate from non-stimulant use to stimulant use was calibrated to reproduce the same prevalence of stimulant use by group in each of the selected epidemic fits used in the main analysis (the Matlab lsqnonlin solver was used to determine this rate).

The results for the proportion of new HIV infections and suicide deaths occurring among MSM/TW who use stimulants was virtually unchanged at 11.1% (9.7-13.3) and 39.1% (17.6-60.0), respectively. Similarly, the proportion of HIV infections averted under the PrEP prioritization by stimulant use scenario was very similar to the baseline analysis (17.5% (9.0-34.0) versus 17.9% (9.1-34.9), respectively), and so was the impact of the random PrEP allocation scenario (15.0% (7.4-30.2) vs respectively). The relative increased impact of the PrEP prioritization scenario was 17% (9-31) under this shorter duration of stimulant use, indicating a strategy of

prioritization by stimulant use may be slightly less effective under short durations of stimulant use, although the difference is small.

Lower PrEP adherence among MSM/TW who use stimulants. While evidence is mixed,[126] some studies have found lower adherence to PrEP among MSM/TW who use stimulants compared to those who do not.[127,128] We used findings from the most recent study assessing this question among MSM/TW participating in the IPrEX open label extension study to inform our sensitivity analysis.[127] Cocaine use was measured in scalp hair samples and categorized as light (500-3000 pg/mg) and moderate to heavy (>3000 pg/mg). PrEP adherence in the first 3 months was measured through plasma tenofovir concentrations. Light cocaine use was associated with 2.10 (95% confidence interval: 1.07 to 4.14) greater odds of having levels of tenofovir below the level of quantitation and the odds were 2.32 (95%CI 1.08 to 5.00) greater among participants with moderate to heavy use, compared to no cocaine use. We used the higher odds ratio and translated it into a relative risk based on the following equation:

RR=OR/((1-p)+(pxOR)), where OR corresponds to the odds ratio for low adherence among MSM/TW who use stimulants and p corresponds to the proportion of MSM/TW who used stimulants in the IPrEX OLE sub-study (100 out of 400 participants).

RR=2.32/((1-0.25)+(0.25*2.32))

RR=1.74

In our main analysis, 84% were assumed to be in the high adherence group, 8% in the medium adherence group and 8% in the low adherence group. In our sensitivity analysis, we assumed that 16%*1.74=27% of MSM/TW who use stimulants would be in the medium or low adherence groups (versus 16% in the main analysis). This resulted in 73%, 8% and 19% of MSM/TW using stimulants in the high, medium and low adherence a group (based on the conservative assumption that all those with undetectable tenofovir had low adherence). Under these assumptions, 16.4% (8.3-32.0) of new HIV infections were averted in the PrEP prioritization by stimulant use scenario and 14.7% (7.3-29.6) under random PrEP allocation. This translated into 11% (3-22) more infections averted under through prioritization by stimulant use versus 19% (11-31) in our baseline scenario assuming no differences in adherence. These findings indicate that while lower adherence to PrEP among MSM/TW who use stimulants might substantially decrease the relative effectiveness of a program prioritizing MSM/TW who use stimulants, the strategy would still likely prevent a higher number of new infections. These findings will vary depending on baseline levels of adherence between settings and therefore similar modelling exercises should be

undertaken to inform decision making in terms of PrEP allocation by stimulant use and implementation of PrEP adherence support programmes for MSM/TW who use stimulants.

Webappendix I: Details of literature search on other harms elevated among people who use stimulants extra-medically

Fatal overdose/poisoning

Amphetamine-type stimulants

Review of reviews (conducted 22 February 2018)

Medline search results

#	Searches	Results
1	(Amphet* or methamphet*).ti,ab. or exp amphetamine/ or exp methamphetamine/	36981
2	((acute and toxic$) or overdos$).ti,ab.	68590
3	1 and 2	632
4	limit 3 to (humans and yr="2000 -Current" and "review")	89

Embase search results

#	Searches	Results
1	(Amphet* or methamphet*).ti,ab. or exp amphetamine/ or exp methamphetamine/	61164
2	((acute and toxic$) or overdos$).ti,ab.	120619
3	1 and 2	1406
4	limit 3 to (human and yr="2000 -Current" and "review")	131

Review of individual papers

Embase search results

#	Searches	Results
1	(amphet$ or methamphet$).ti,ab. or exp amphetamine/ or exp methamphetamine/	61164
2	((acute and toxic$) or overdos$).ti,ab.	120619
3	1 and 2	1406
4	limit 3 to (human and yr="2000 -Current")	797

Cocaine

Review of reviews

Medline search results

#	Searches	Results
1	(Cocaine$).ti,ab. or exp Cocaine/ or exp cocaine dependence/ or exp cocaine derivative/	37171
2	((acute and toxic$) or overdos$).ti,ab.	68530
3	1 and 2	902
4	limit 3 to (human and yr="2000 -Current" and 'review')	87

Embase search results

#	Searches	Results
1	(Cocaine$).ti,ab. or exp Cocaine/ or exp cocaine dependence/ or exp cocaine derivative/	63755
2	((acute and toxic$) or overdos$).ti,ab.	120619

#	Searches	Results
3	1 and 2	1886
4	limit 3 to (human and yr="2000 -Current" and 'review')	191

Review of individual papers

Embase search results

#	Searches	Results
1	(Cocaine$).ti,ab. or exp Cocaine/ or exp cocaine dependence/ or exp cocaine derivative/	63755
2	((acute and toxic$) or overdos$).ti,ab.	120619
3	1 and 2	1886
4	limit 3 to (human and yr="2000 -Current")	1199

Accidental injury

Amphetamine-type stimulants

Review of reviews

Medline search results

#	Searches	Results
1	(Amphet* or methamphet*).ti,ab. or exp amphetamine/ or exp methamphetamine/	36981
2	accident$.ti,ab.	90211
3	1 and 2	246
4	limit 3 to (humans and yr="2000 -Current" and "review")	31

Embase search results

#	Searches	Results
1	(Amphet* or methamphet*).ti,ab. or exp amphetamine/ or exp methamphetamine/	61164
2	accident$.ti,ab.	147679
3	1 and 2	496
4	limit 3 to (human and yr="2000 -Current" and "review")	60

Review of individual papers

Embase search results

#	Searches	Results
1	(Amphet* or methamphet*).ti,ab. or exp amphetamine/ or exp methamphetamine/	61164
2	accident$.ti,ab.	147679
3	1 and 2	496
4	limit 3 to yr="2000 -Current"	338

Cocaine

Review of reviews

Medline search results

#	Searches	Results

1	cocaine*.ti,ab. or exp Cocaine/ or exp cocaine dependence/ or exp cocaine derivative/	37171
2	accident$.ti,ab.	90147
3	1 and 2	311
4	limit 3 to (human and yr="2000 -Current" and 'review')	32

Embase search results

#	Searches	Results
1	cocaine*.ti,ab. or exp Cocaine/ or exp cocaine dependence/ or exp cocaine derivative/	63755
2	accident$.ti,ab.	147679
3	1 and 2	609
4	limit 3 to (human and yr="2000 -Current" and 'review')	70

Review of individual papers

Embase search results

#	Searches	Results
1	cocaine*.ti,ab. or exp Cocaine/ or exp cocaine dependence/ or exp cocaine derivative/	63755
2	accident$.ti,ab.	147679
3	1 and 2	609
4	limit 3 to (human and yr="2000 -Current")	389

Motor vehicle accidents/transport injuries

Amphetamine-type stimulants

Review of reviews

Medline search results

#	Searches	Results
1	(Amphet* or methamphet*).ti,ab. or exp amphetamine/ or exp methamphetamine/	36981
2	(accident$ and vehicle$).ti,ab.	6728
3	1 and 2	21
4	limit 3 to (humans and yr="2000 -Current" and "review")	2

Embase search results

#	Searches	Results
1	(Amphet* or methamphet*).ti,ab. or exp amphetamine/ or exp methamphetamine/	61164
2	(accident$ and vehicle$).ti,ab.	10308
3	1 and 2	42
4	limit 3 to (human and yr="2000 -Current" and "review")	5

Review of individual papers

Embase search results

#	Searches	Results
1	(amphet$ or methamphet$).ti,ab. or exp amphetamine/ or exp methamphetamine/	61164

#	Searches	Results
2	(accident$ and vehicle$).ti,ab.	10308
3	1 and 2	42
4	limit 3 to (human and yr="2000 -Current")	35

Cocaine

Review of reviews

Medline search results

#	Searches	Results
1	Cocaine$.ti,ab. or exp Cocaine/ or exp cocaine dependence/ or exp cocaine derivative/	37171
2	(accident$ and vehicle$).ti,ab.	6723
3	1 and 2	34
4	limit 3 to (human and yr="2000 -Current" and 'review')	2

Embase search results

#	Searches	Results
1	Cocaine$.ti,ab. or exp Cocaine/ or exp cocaine dependence/ or exp cocaine derivative/	63755
2	(accident$ and vehicle$).ti,ab.	10308
3	1 and 2	59
4	limit 3 to (human and yr="2000 -Current" and 'review')	5

Review of individual papers

Embase search results

#	Searches	Results
1	Cocaine$.ti,ab. or exp Cocaine/ or exp cocaine dependence/ or exp cocaine derivative/	63755
2	(accident$ and vehicle$).ti,ab.	10308
3	1 and 2	59
4	limit 3 to (human and yr="2000 -Current")	38

Drug-induced psychotic symptoms

Amphetamine-type stimulants

Review of reviews

Medline search results

#	Searches	Results
1	(Amphet* or methamphet*).ti,ab. or exp amphetamine/ or exp methamphetamine/	36981
2	(psychosis or psychotic).ti,ab. or exp Drug Induced Psychosis/	45295
3	1 and 2	1157
4	limit 3 to (humans and yr="2000 -Current" and "review")	133

Embase search results

#	Searches	Results
1	(Amphet* or methamphet*).ti,ab. or exp amphetamine/ or exp methamphetamine/	61164

#	Searches	Results
2	(psychosis or psychotic).ti,ab. or exp Drug Induced Psychosis/	82785
3	1 and 2	2210
4	limit 3 to (human and yr="2000 -Current" and "review")	233

Review of individual papers

Embase search results

#	Searches	Results
1	(Amphet* or methamphet*).ti,ab. or exp amphetamine/ or exp methamphetamine/	61164
2	(psychosis or psychotic).ti,ab.	82749
3	exp drug induced psychosis/	168
4	2 or 3	82785
5	1 and 4	2210
6	limit 5 to (human and yr="2000 -Current")	1064

Cocaine

Review of reviews

Medline search results

#	Searches	Results
1	cocaine*.ti,ab. or exp Cocaine/ or exp cocaine dependence/ or exp cocaine derivative/	37171
2	(psychosis or psychotic).ti,ab. or exp Drug Induced Psychosis/	45254
3	1 and 2	420
4	limit 3 to (human and yr="2000 -Current" and 'review')	44

Embase search results

#	Searches	Results
1	cocaine*.ti,ab. or exp Cocaine/ or exp cocaine dependence/ or exp cocaine derivative/	63755
2	(psychosis or psychotic).ti,ab. or exp Drug Induced Psychosis/	82785
3	1 and 2	989
4	limit 3 to (human and yr="2000 -Current" and 'review')	130

Review of individual papers

Embase search results

#	Searches	Results
1	cocaine*.ti,ab. or exp Cocaine/ or exp cocaine dependence/ or exp cocaine derivative/	63755
2	(psychosis or psychotic).ti,ab. or Drug Induced Psychosis/	82757
3	1 and 2	986
4	limit 3 to (human and yr="2000 -Current")	647

Myocardial infarction

Amphetamine-type stimulants

Review of reviews

Medline search results

#	Searches	Results
1	(Amphet* or methamphet*).ti,ab. or exp amphetamine/ or exp methamphetamine/	36981
2	myocardial infarction.ti,ab. or exp Heart Infarction/	145537
3	1 and 2	97
4	limit 3 to (humans and yr="2000 -Current" and "review")	20

Embase search results

#	Searches	Results
1	(Amphet* or methamphet*).ti,ab. or exp amphetamine/ or exp methamphetamine/	61164
2	myocardial infarction.ti,ab. or exp Heart Infarction/	390225
3	1 and 2	438
4	limit 3 to (human and yr="2000 -Current" and "review")	110

Review of individual papers

Embase search results

#	Searches	Results
1	(amphet$ or methamphet$).ti,ab. or exp amphetamine/ or exp methamphetamine/	61164
2	myocardial infarction.ti,ab. or exp Heart Infarction/	390225
3	1 and 2	438
4	limit 3 to (human and yr="2000 -Current")	369

Cocaine

Review of reviews

Medline search results

#	Searches	Results
1	Cocaine$.ti,ab. or exp Cocaine/ or exp cocaine dependence/ or exp cocaine derivative/	37171
2	myocardial infarction.ti,ab. or exp Heart Infarction/	145455
3	1 and 2	404
4	limit 3 to (human and yr="2000 -Current" and 'review'	52

Embase search results

#	Searches	Results
1	Cocaine$.ti,ab. or exp Cocaine/ or exp cocaine dependence/ or exp cocaine derivative/	63755
2	myocardial infarction.ti,ab. or exp Heart Infarction/	390225
3	1 and 2	1137
4	limit 3 to (human and yr="2000 -Current" and 'review'	192

Review of individual papers

Embase search results

#	Searches	Results
1	Cocaine$.ti,ab. or exp Cocaine/ or exp cocaine dependence/ or exp cocaine derivative/	63755
2	myocardial infarction.ti,ab. or exp Heart Infarction/	390225
3	1 and 2	1137
4	limit 3 to (human and yr="2000 -Current")	785

Dependence

Amphetamine-type stimulants

Review of reviews

Medline search results

#	Searches	Results
1	(Amphet* or methamphet*).ti,ab. or exp amphetamine/ or exp methamphetamine/	36981
2	((dependen$ or use-disorder) and risk).ti,ab.	64961
3	1 and 2	382
4	limit 3 to (humans and yr="2000 -Current" and "review")	53

Embase search results

#	Searches	Results
1	(Amphet* or methamphet*).ti,ab. or exp amphetamine/ or exp methamphetamine/	61164
2	((dependen$ or use-disorder) and risk).ti,ab.	107724
3	1 and 2	858
4	limit 3 to (human and yr="2000 -Current" and "review")	101

Review of individual papers

Embase search results

#	Searches	Results
1	(Amphet* or methamphet*).ti,ab. or exp amphetamine/ or exp methamphetamine/	61164
2	(dependen$ or use-disorder).ti,ab.	1777267
3	risk.ti,ab.	2453184
4	2 and 3	107724
5	1 and 4	858
6	limit 5 to (human and yr="2000 -Current")	671

Cocaine

Review of reviews

Medline search results

#	Searches	Results
1	cocaine*.ti,ab. or exp Cocaine/ or exp cocaine dependence/ or exp cocaine derivative/	37171
2	((dependen$ or use-disorder) and risk).ti,ab.	64858

#	Searches	Results
3	1 and 2	789
4	limit 3 to (human and yr="2000 -Current" and 'review'	79

Embase search results

#	Searches	Results
1	cocaine*.ti,ab. or exp Cocaine/ or exp cocaine dependence/ or exp cocaine derivative/	63755
2	((dependen$ or use-disorder) and risk).ti,ab.	107724
3	1 and 2	1609
4	limit 3 to (human and yr="2000 -Current" and 'review'	155

Review of individual papers

Embase search results

#	Searches	Results
1	cocaine*.ti,ab. or exp Cocaine/ or exp cocaine dependence/ or exp cocaine derivative/	63755
2	((dependen$ or use-disorder) and risk).ti,ab.	107724
3	1 and 2	1609
4	limit 3 to (human and yr="2000 -Current")	1295

Circulatory system disease

Amphetamine-type stimulants

Review of reviews

Cardiovascular pathology

Medline search results

#	Searches	Results
1	(Amphet* or methamphet*).ti,ab. or exp amphetamine/ or exp methamphetamine/	36981
2	(cardio$ or stroke or heart-disease or blood-pressure or hypoxi$).ti,ab.	1060972
3	1 and 2	1205
4	limit 3 to (humans and yr="2000 -Current" and "review")	186

Embase search results

#	Searches	Results
1	(Amphet* or methamphet*).ti,ab. or exp amphetamine/ or exp methamphetamine/	61164
2	(cardio$ or stroke or heart-disease or blood-pressure or hypoxi$).ti,ab.	1757440
3	1 and 2	2616
4	limit 3 to (human and yr="2000 -Current" and "review")	416

Pulmonary disease

Medline search results

#	Searches	Results
1	(Amphet* or methamphet*).ti,ab. or exp amphetamine/ or exp methamphetamine/	36981
2	(pulmonary disease or pulmonary or lung).ti,ab.	779212

#	Searches	Results
3	1 and 2	262
4	limit 3 to (humans and yr="2000 -Current" and "review")	31

Embase search results

#	Searches	Results
1	(Amphet* or methamphet*).ti,ab. or exp amphetamine/ or exp methamphetamine/	61164
2	(pulmonary disease or pulmonary or lung).ti,ab.	1256882
3	1 and 2	587
4	limit 3 to (human and yr="2000 -Current" and "review")	62

Review of individual papers

Embase search results

#	Searches	Results
1	(amphet$ or methamphet$).ti,ab. or exp amphetamine/ or exp methamphetamine/	61164
2	(cardio$ or stroke or heart-disease or blood-pressure or hypoxi$).ti,ab.	1757440
3	(pulmonary disease or pulmonary or lung).ti,ab.	1256882
4	2 or 3	2867137
5	1 and 4	3035
6	limit 5 to (human and yr="2000 -Current")	1634

Cocaine

Review of reviews

Cardiovascular pathology

Medline search results

#	Searches	Results
1	Cocaine$.ti,ab. or exp Cocaine/ or exp cocaine dependence/ or exp cocaine derivative/	37171
2	(cardio$ or stroke or heart-disease or blood-pressure or hypoxi$).ti,ab.	1059985
3	1 and 2	1900
4	limit 3 to (human and yr="2000 -Current" and 'review'	199

Embase search results

#	Searches	Results
1	Cocaine$.ti,ab. or exp Cocaine/ or exp cocaine dependence/ or exp cocaine derivative/	63755
2	(cardio$ or stroke or heart-disease or blood-pressure or hypoxi$).ti,ab.	1757440
3	1 and 2	3665
4	limit 3 to (human and yr="2000 -Current" and 'review'	460

Pulmonary disease

Medline search results

#	Searches	Results
1	Cocaine$.ti,ab. or exp Cocaine/ or exp cocaine dependence/ or exp cocaine derivative/	37171
2	(cardio$ or stroke or heart-disease or blood-pressure or hypoxi$).ti,ab.	778549
3	1 and 2	496
4	limit 3 to (human and yr="2000 -Current" and 'review'	48

Embase search results

#	Searches	Results
1	Cocaine$.ti,ab. or exp Cocaine/ or exp cocaine dependence/ or exp cocaine derivative/	63755
2	(cardio$ or stroke or heart-disease or blood-pressure or hypoxi$).ti,ab.	1256882
3	1 and 2	1146
4	limit 3 to (human and yr="2000 -Current" and 'review'	110

Review of individual papers

Embase search results

#	Searches	Results
1	Cocaine$.ti,ab. or exp Cocaine/ or exp cocaine dependence/ or exp cocaine derivative/	63755
2	(cardio$ or stroke or heart-disease or blood-pressure or hypoxi$).ti,ab.	1757440
3	(pulmonary disease or pulmonary or lung).ti,ab.	1256882
4	2 or 3	2867137
5	1 and 4	4549
6	limit 5 to (human and yr="2000 -Current")	2319

Blood diseases

Amphetamine-type stimulants

Review of reviews

Liver disease (cirrhosis)

Medline search results

#	Searches	Results
1	(Amphet* or methamphet*).ti,ab. or exp amphetamine/ or exp methamphetamine/	36981
2	(liver disease or liver or cirrhosis).ti,ab.	678452
3	1 and 2	575
4	limit 3 to (humans and yr="2000 -Current" and "review")	16

Embase search results

#	Searches	Results
1	(Amphet* or methamphet*).ti,ab. or exp amphetamine/ or exp methamphetamine/	61164
2	(liver disease or liver or cirrhosis).ti,ab.	1052617
3	1 and 2	914
4	limit 3 to (human and yr="2000 -Current" and "review")	49

Anemia

Medline search results

#	Searches	Results
1	(Amphet* or methamphet*).ti,ab. or exp amphetamine/ or exp methamphetamine/	36981
2	(an*emia or iron).ti,ab.	236692
3	1 and 2	95
4	limit 3 to (humans and yr="2000 -Current" and "review")	10

Embase search results

#	Searches	Results
1	(Amphet* or methamphet*).ti,ab. or exp amphetamine/ or exp methamphetamine/	61164
2	(an*emia or iron).ti,ab.	379124
3	1 and 2	161
4	limit 3 to (human and yr="2000 -Current" and "review")	13

Hypercholestermia

Medline search results

#	Searches	Results
1	(Amphet* or methamphet*).ti,ab. or exp amphetamine/ or exp methamphetamine/	36981
2	(hypercholestermia or cholesterol).ti,ab.	197300
3	1 and 2	50
4	limit 3 to (humans and yr="2000 -Current" and "review")	6

Embase search results

#	Searches	Results
1	(Amphet* or methamphet*).ti,ab. or exp amphetamine/ or exp methamphetamine/	61164
2	(hypercholestermia or cholesterol).ti,ab.	297183
3	1 and 2	100
4	limit 3 to (human and yr="2000 -Current" and "review")	7

Lipodystrophy

Medline search results

#	Searches	Results
1	(Amphet* or methamphet*).ti,ab. or exp amphetamine/ or exp methamphetamine/	36981
2	lipodystrophy.ti,ab.	3750
3	1 and 2	0
4	limit 3 to (human and yr="2000 -Current" and "review")	0

Embase search results

#	Searches	Results
1	(Amphet* or methamphet*).ti,ab. or exp amphetamine/ or exp methamphetamine/	61164
2	lipodystrophy.ti,ab.	5479

3	1 and 2	3
4	limit 3 to (human and yr="2000 -Current" and "review")	0

Diabetes

Medline search results

#	Searches	Results
1	(Amphet* or methamphet*).ti,ab. or exp amphetamine/ or exp methamphetamine/	36981
2	(diabetes or insulin).ti,ab.	574154
3	1 and 2	278
4	limit 3 to (human and yr="2000 -Current" and "review")	42

Embase search results

#	Searches	Results
1	(Amphet* or methamphet*).ti,ab. or exp amphetamine/ or exp methamphetamine/	61164
2	(diabetes or insulin).ti,ab.	937088
3	1 and 2	617
4	limit 3 to (human and yr="2000 -Current" and "review")	92

Cancers

Medline search results

#	Searches	Results
1	(Amphet* or methamphet*).ti,ab. or exp amphetamine/ or exp methamphetamine/	36981
2	cancer$.ti,ab.	1284897
3	1 and 2	95
4	limit 3 to (human and yr="2000 -Current" and "review")	22

Embase search results

#	Searches	Results
1	(Amphet* or methamphet*).ti,ab. or exp amphetamine/ or exp methamphetamine/	61164
2	cancer$.ti,ab.	2093097
3	1 and 2	291
4	limit 3 to (human and yr="2000 -Current" and "review")	77

Review of individual papers

Embase search results

#	Searches	Results
1	(Amphet* or methamphet*).ti,ab. or exp amphetamine/ or exp methamphetamine/	61164
2	(liver disease or liver or cirrhosis).ti,ab.	1052617
3	(an*emia or iron).ti,ab.	379124
4	(hypercholestermia or cholesterol).ti,ab.	297183
5	lipodystrophy.ti,ab.	5479
6	(diabetes or insulin).ti,ab.	937088
7	cancer$.ti,ab.	2093097

#	Searches	Results
8	2 or 3 or 4 or 5 or 6 or 7	4368162
9	1 and 8	1967
10	limit 9 to (human and yr="2000 -Current")	832

Cocaine

Review of reviews

Liver disease (cirrhosis)

Medline search results

#	Searches	Results
1	Cocaine$.ti,ab. or exp Cocaine/ or exp cocaine dependence/ or exp cocaine derivative/	37171
2	(liver disease OR liver OR cirrhosis).ti,ab	678003
3	1 and 2	484
4	limit 3 to (human and yr="2000 -Current" and 'review'	30

Embase search results

#	Searches	Results
1	Cocaine$.ti,ab. or exp Cocaine/ or exp cocaine dependence/ or exp cocaine derivative/	63755
2	(liver disease OR liver OR cirrhosis).ti,ab	1052617
3	1 and 2	988
4	limit 3 to (human and yr="2000 -Current" and 'review'	93

Anemia

Medline search results

#	Searches	Results
1	Cocaine$.ti,ab. or exp Cocaine/ or exp cocaine dependence/ or exp cocaine derivative/	37171
2	(an*emia OR iron).ti,ab	236537
3	1 and 2	78
4	limit 3 to (human and yr="2000 -Current" and 'review'	9

Embase search results

#	Searches	Results
1	Cocaine$.ti,ab. or exp Cocaine/ or exp cocaine dependence/ or exp cocaine derivative/	63755
2	(an*emia OR iron).ti,ab	379124
3	1 and 2	192
4	limit 3 to (human and yr="2000 -Current" and 'review'	20

Hypercholestermia

Medline search results

#	Searches	Results
1	Cocaine$.ti,ab. or exp Cocaine/ or exp cocaine dependence/ or exp cocaine derivative/	37171
2	(hypercholestermia OR cholesterol).ti,ab	197167
3	1 and 2	73

4	limit 3 to (human and yr="2000 -Current" and 'review'	9

Embase search results

#	Searches	Results
1	Cocaine$.ti,ab. or exp Cocaine/ or exp cocaine dependence/ or exp cocaine derivative/	63755
2	(hypercholestermia OR cholesterol).ti,ab	297183
3	1 and 2	128
4	limit 3 to (human and yr="2000 -Current" and 'review'	8

Lipodystrophy

Medline search results

#	Searches	Results
1	Cocaine$.ti,ab. or exp Cocaine/ or exp cocaine dependence/ or exp cocaine derivative/	37171
2	lipodystrophy.ti,ab	3748
3	1 and 2	1
4	limit 3 to (human and yr="2000 -Current" and 'review'	0

Embase search results

#	Searches	Results
1	Cocaine$.ti,ab. or exp Cocaine/ or exp cocaine dependence/ or exp cocaine derivative/	63755
2	lipodystrophy.ti,ab	5479
3	1 and 2	4
4	limit 3 to (human and yr="2000 -Current" and 'review'	2

Diabetes

Medline search results

#	Searches	Results
1	Cocaine$.ti,ab. or exp Cocaine/ or exp cocaine dependence/ or exp cocaine derivative/	37171
2	(diabetes OR insulin).ti,ab	573552
3	1 and 2	313
4	limit 3 to (human and yr="2000 -Current" and 'review'	48

Embase search results

#	Searches	Results
1	Cocaine$.ti,ab. or exp Cocaine/ or exp cocaine dependence/ or exp cocaine derivative/	63755
2	(diabetes OR insulin).ti,ab	937088
3	1 and 2	723
4	limit 3 to (human and yr="2000 -Current" and 'review'	110

Cancers

Medline search results

#	Searches	Results
1	Cocaine$.ti,ab. or exp Cocaine/ or exp cocaine dependence/ or exp cocaine derivative/	37171

#	Searches	Results
2	cancer$.ti,ab	1283034
3	1 and 2	144
4	limit 3 to (human and yr="2000 -Current" and 'review'	34

Embase search results

#	Searches	Results
1	Cocaine$.ti,ab. or exp Cocaine/ or exp cocaine dependence/ or exp cocaine derivative/	63755
2	cancer$.ti,ab	2093097
3	1 and 2	431
4	limit 3 to (human and yr="2000 -Current" and 'review'	103

Review of individual papers

Embase search results

#	Searches	Results
1	cocaine*.ti,ab. or exp Cocaine/ or exp cocaine dependence/ or exp cocaine derivative/	63755
2	(liver disease or liver or cirrhosis).ti,ab.	1052617
3	(an*emia or iron).ti,ab.	379124
4	(hypercholestermia or cholesterol).ti,ab.	297183
5	lipodystrophy.ti,ab.	5479
6	(diabetes or insulin).ti,ab.	937088
7	cancer$.ti,ab.	2093097
8	2 or 3 or 4 or 5 or 6 or 7	4368162
9	1 and 8	2259
10	limit 9 to (human and yr="2000 -Current")	1269

Psychotic disorders (schizophrenia)

Amphetamine-type stimulants

Review of reviews

Medline search results

#	Searches	Results
1	(Amphet* or methamphet*).ti,ab. or exp amphetamine/ or exp methamphetamine/	36981
2	(Schizophren$ or psychotic).ti,ab.	114622
3	1 and 2	1818
4	limit 3 to (human and yr="2000 -Current" and "review")	157

Embase search results

#	Searches	Results
1	(Amphet* or methamphet*).ti,ab. or exp amphetamine/ or exp methamphetamine/	61164
2	(Schizophren$ or psychotic).ti,ab.	182993
3	1 and 2	3426
4	limit 3 to (human and yr="2000 -Current" and "review")	365

Review of individual papers

Embase search results

#	Searches	Results
1	(amphet$ or methamphet$).ti,ab. or exp amphetamine/ or exp methamphetamine/	61164
2	(Schizophren$ or psychotic).ti,ab.	182993
3	1 and 2	3426
4	limit 3 to (human and yr="2000 -Current")	1389

Cocaine

Review of reviews

Medline search results

#	Searches	Results
1	Cocaine$.ti,ab. or exp Cocaine/ or exp cocaine dependence/ or exp cocaine derivative/	37171
2	(Schizophren$ or psychotic).ti,ab.	114524
3	1 and 2	637
4	limit 3 to (human and yr="2000 -Current" and 'review'	92

Embase search results

#	Searches	Results
1	Cocaine$.ti,ab. or exp Cocaine/ or exp cocaine dependence/ or exp cocaine derivative/	63755
2	(Schizophren$ or psychotic).ti,ab.	182993
3	1 and 2	1477
4	limit 3 to (human and yr="2000 -Current" and 'review'	269

Review of individual papers

Embase search results

#	Searches	Results
1	Cocaine$.ti,ab. or exp Cocaine/ or exp cocaine dependence/ or exp cocaine derivative/	63755
2	(Schizophren$ or psychotic).ti,ab.	182993
3	1 and 2	1477
4	limit 3 to (human and yr="2000 -Current")	972

Common mental disorders (depression, anxiety)

Amphetamine-type stimulants

Review of reviews

Medline search results

#	Searches	Results
1	(Amphet* or methamphet*).ti,ab. or exp amphetamine/ or exp methamphetamine/	36981
2	(depress$ or anxiety).ti,ab.	423928
3	1 and 2	2312
4	limit 3 to (human and yr="2000 -Current" and "review")	155

Embase search results

#	Searches	Results
1	(Amphet* or methamphet*).ti,ab. or exp amphetamine/ or exp methamphetamine/	61164
2	(depress$ or anxiety).ti,ab.	671973
3	1 and 2	4756
4	limit 3 to (human and yr="2000 -Current" and "review")	466

Review of individual papers

Embase search results

#	Searches	Results
1	(amphet$ or methamphet$).ti,ab. or exp amphetamine/ or exp methamphetamine/	61164
2	(depress$ or anxiety).ti,ab.	671973
3	1 and 2	4756
4	limit 3 to (human and yr="2000 -Current")	1809

Cocaine

Review of reviews

Medline search results

#	Searches	Results
1	Cocaine$.ti,ab. or exp Cocaine/ or exp cocaine dependence/ or exp cocaine derivative/	37171
2	(depress$ or anxiety).ti,ab.	423440
3	1 and 2	2291
4	limit 3 to (human and yr="2000 -Current" and 'review'	178

Embase search results

#	Searches	Results
1	Cocaine$.ti,ab. or exp Cocaine/ or exp cocaine dependence/ or exp cocaine derivative/	63755
2	(depress$ or anxiety).ti,ab.	671973
3	1 and 2	4461
4	limit 3 to (human and yr="2000 -Current" and 'review'	450

Review of individual papers

Embase search results

#	Searches	Results
1	Cocaine$.ti,ab. or exp Cocaine/ or exp cocaine dependence/ or exp cocaine derivative/	63755
2	(depress$ or anxiety).ti,ab.	671973
3	1 and 2	4461
4	limit 3 to (human and yr="2000 -Current")	2311

Other mental health and substance use disorders

Amphetamine-type stimulants

Review of reviews

Medline search results

#	Searches	Results
1	(Amphet* or methamphet*).ti,ab. or exp amphetamine/ or exp methamphetamine/	36981
2	(mental health or disorder$).ti,ab.	888845
3	1 and 2	3439
4	limit 3 to (human and yr="2000 -Current" and "review")	581

Embase search results

#	Searches	Results
1	(Amphet* or methamphet*).ti,ab. or exp amphetamine/ or exp methamphetamine/	61164
2	(mental health or disorder$).ti,ab.	1416978
3	1 and 2	8023
4	limit 3 to (human and yr="2000 -Current" and "review")	1708

Review of individual papers

Embase search results

#	Searches	Results
1	(amphet$ or methamphet$).ti,ab. or exp amphetamine/ or exp methamphetamine/	61164
2	(mental health or disorder$).ti,ab.	1416978
3	1 and 2	8023
4	limit 3 to (human and yr="2000 -Current")	5332

Cocaine

Review of reviews

Medline search results

#	Searches	Results
1	Cocaine$.ti,ab. or exp Cocaine/ or exp cocaine dependence/ or exp cocaine derivative/	37171
2	(mental health or disorder$).ti,ab.	887707
3	1 and 2	3402
4	limit 3 to (human and yr="2000 -Current" and 'review')	542

Embase search results

#	Searches	Results
1	Cocaine$.ti,ab. or exp Cocaine/ or exp cocaine dependence/ or exp cocaine derivative/	63755
2	(mental health or disorder$).ti,ab.	1416978
3	1 and 2	7887
4	limit 3 to (human and yr="2000 -Current" and 'review')	1410

Review of individual papers

Embase search results

#	Searches	Results
1	Cocaine$.ti,ab. or exp Cocaine/ or exp cocaine dependence/ or exp cocaine derivative/	63755
2	(mental health or disorder$).ti,ab.	1416978
3	1 and 2	7887
4	limit 3 to (human and yr="2000 -Current")	5727

Alzheimer's disease and other dementias

Amphetamine-type stimulants

Review of reviews

Medline search results

#	Searches	Results
1	(Amphet* or methamphet*).ti,ab. or exp amphetamine/ or exp methamphetamine/	36981
2	exp Alzheimer disease/ or alzheim*.ti,ab.	116777
3	1 and 2	107
4	limit 3 to (human and yr="2000 -Current" and "review")	28

Embase search results

#	Searches	Results
1	(Amphet* or methamphet*).ti,ab. or exp amphetamine/ or exp methamphetamine/	61164
2	exp Alzheimer disease/ or alzheim*.ti,ab.	199452
3	1 and 2	407
4	limit 3 to (human and yr="2000 -Current" and "review")	143

Review of individual papers

Embase search results

#	Searches	Results
1	(amphet$ or methamphet$).ti,ab. or exp amphetamine/ or exp methamphetamine/	61164
2	exp Alzheimer disease/ or alzheim*.ti,ab.	199452
3	1 and 2	407
4	limit 3 to (human and yr="2000 -Current")	274

Cocaine

Review of reviews

Medline search results

#	Searches	Results
1	Cocaine$.ti,ab. or exp Cocaine/ or exp cocaine dependence/ or exp cocaine derivative/	37171
2	exp Alzheimer disease/ or alzheim*.ti,ab.	116576
3	1 and 2	66
4	limit 3 to (human and yr="2000 -Current")	23

Embase search results

#	Searches	Results
1	Cocaine$.ti,ab. or exp Cocaine/ or exp cocaine dependence/ or exp cocaine derivative/	63755
2	exp Alzheimer disease/ or alzheim*.ti,ab.	199452
3	1 and 2	278
4	limit 3 to (human and yr="2000 -Current")	116

Review of individual papers

Embase search results

#	Searches	Results
1	Cocaine$.ti,ab. or exp Cocaine/ or exp cocaine dependence/ or exp cocaine derivative/	63755
2	exp Alzheimer disease/ or alzheim*.ti,ab.	199452
3	1 and 2	278
4	limit 3 to (human and yr="2000 -Current")	212

Diseases of the respiratory system

Amphetamine-type stimulants

Review of reviews

Respiratory infection

Medline search results

#	Searches	Results
1	(Amphet* or methamphet*).ti,ab. or exp amphetamine/ or exp methamphetamine/	36981
2	exp Respiratory Tract Infection/ or respira* infect*.ti,ab.	339800
3	1 and 2	49
4	limit 3 to (human and yr="2000 -Current" and "review")	2

Embase search results

#	Searches	Results
1	(Amphet* or methamphet*).ti,ab. or exp amphetamine/ or exp methamphetamine/	61164
2	exp Respiratory Tract Infection/ or respira* infect*.ti,ab.	414815
3	1 and 2	243
4	limit 3 to (human and yr="2000 -Current" and "review")	80

Asthma

Medline search results

#	Searches	Results
1	(Amphet* or methamphet*).ti,ab. or exp amphetamine/ or exp methamphetamine/	36981
2	exp Asthma/ or asthma*.ti,ab.	149531
3	1 and 2	42
4	limit 3 to (human and yr="2000 -Current" and "review")	5

Embase search results

#	Searches	Results
1	(Amphet* or methamphet*).ti,ab. or exp amphetamine/ or exp methamphetamine/	61164
2	exp Asthma/ or asthma*.ti,ab.	273616
3	1 and 2	187
4	limit 3 to (human and yr="2000 -Current" and "review")	42

Lung disease

Medline search results

#	Searches	Results
1	(Amphet* or methamphet*).ti,ab. or exp amphetamine/ or exp methamphetamine/	36981
2	exp Lung Disease/	804908
3	1 and 2	160
4	limit 3 to (human and yr="2000 -Current" and "review")	19

Embase search results

#	Searches	Results
1	(Amphet* or methamphet*).ti,ab. or exp amphetamine/ or exp methamphetamine/	61164
2	exp Lung Disease/	1258249
3	1 and 2	843
4	limit 3 to (human and yr="2000 -Current" and "review")	199

Decreased lung function

Medline search results

#	Searches	Results
1	(Amphet* or methamphet*).ti,ab. or exp amphetamine/ or exp methamphetamine/	36981
2	exp Respiratory Function Tests/ or (lung and function).ti,ab.	258210
3	1 and 2	42
4	limit 3 to (full text and humans and yr="2000 -Current" and "review")	1

Embase search results

#	Searches	Results
1	(Amphet* or methamphet*).ti,ab. or exp amphetamine/ or exp methamphetamine/	61164
2	exp Lung Function/	130329
3	1 and 2	45
4	limit 3 to (human and yr="2000 -Current" and "review")	11

Review of individual papers

Embase search results

#	Searches	Results
1	(Amphet* or methamphet*).ti,ab. or exp amphetamine/ or exp methamphetamine/	61164
2	exp respiratory tract infection/	408246

3	respira* infect*.ti,ab.	28769
4	exp Asthma/ or asthma*.ti,ab.	273616
5	exp Lung Disease/	1258249
6	exp Lung Function/	130329
7	2 or 3 or 4 or 5 or 6	1711300
8	1 and 7	1159
9	limit 8 to (human and yr="2000 -Current")	862

Cocaine

Review of reviews

Chronic lower respiratory infections

Medline search results

#	Searches	Results
1	Cocaine$.ti,ab. or exp Cocaine/ or exp cocaine dependence/ or exp cocaine derivative/	37171
2	exp Respiratory Tract Infection/ or respira* infect*.ti,ab.	339611
3	1 and 2	129
4	limit 3 to (human and yr="2000 -Current" and 'review'	7

Embase search results

#	Searches	Results
1	(Cocaine$).ti,ab. or exp Cocaine/ or exp cocaine dependence/ or exp cocaine derivative/	63755
2	exp Respiratory Tract Infection/ or respira* infect*.ti,ab.	414815
3	1 and 2	350
4	limit 3 to (human and yr="2000 -Current" and 'review'	90

Asthma

Medline search results

#	Searches	Results
1	Cocaine$.ti,ab. or exp Cocaine/ or exp cocaine dependence/ or exp cocaine derivative/	37171
2	exp Asthma/ or asthma*.ti,ab.	149437
3	1 and 2	82
4	limit 3 to (human and yr="2000 -Current" and 'review'	11

Embase search results

#	Searches	Results
1	Cocaine$.ti,ab. or exp Cocaine/ or exp cocaine dependence/ or exp cocaine derivative/	63755
2	exp Asthma/ or asthma*.ti,ab.	273616
3	1 and 2	341
4	limit 3 to (human and yr="2000 -Current" and 'review'	77

Lung diseases due to external agents

Medline search results

#	Searches	Results
1	Cocaine$.ti,ab. or exp Cocaine/ or exp cocaine dependence/ or exp cocaine derivative/	37171
2	exp Lung Disease/	804323
3	1 and 2	365
4	limit 3 to (human and yr="2000 -Current" and 'review'	38

Embase search results

#	Searches	Results
1	Cocaine$.ti,ab. or exp Cocaine/ or exp cocaine dependence/ or exp cocaine derivative/	63755
2	exp Lung Disease/	1258249
3	1 and 2	1446
4	limit 3 to (human and yr="2000 -Current" and 'review'	267

Decreased lung function

Medline search results

#	Searches	Results
1	Cocaine$.ti,ab. or exp Cocaine/ or exp cocaine dependence/ or exp cocaine derivative/	37171
2	exp respiratory function tests/ or (lung and function).ti,ab.	258077
3	1 and 2	122
4	limit 3 to (human and yr="2000 -Current" and 'review'	9

Embase search results

#	Searches	Results
1	Cocaine$.ti,ab. or exp Cocaine/ or exp cocaine dependence/ or exp cocaine derivative/	63755
2	exp Digestive System Disease/ or exp Stomach Ulcer/	130329
3	1 and 2	106
4	limit 3 to (human and yr="2000 -Current" and 'review'	20

Review of individual papers

Embase search results

#	Searches	Results
1	Cocaine$.ti,ab. or exp Cocaine/ or exp cocaine dependence/ or exp cocaine derivative/	63755
2	Respiratory Tract Infection/ or respira* infect*.ti,ab.	70061
3	Asthma/ or asthma*.ti,ab.	262514
4	Lung Disease/	81932
5	Lung Function/	73921
6	2 or 3 or 4 or 5	452715
7	1 and 6	520
8	limit 7 to (human and yr="2000 -Current")	388

Diseases of the skin and subcutaneous tissue

Amphetamine-type stimulants

Review of reviews

Abscess or injection site irritation

Medline search results

#	Searches	Results
1	(Amphet* or methamphet*).ti,ab. or exp amphetamine/ or exp methamphetamine/	36981
2	exp Injection site abscess/ or exp Skin Abscess/ or (skin and inject*).ti,ab.	19456
3	1 and 2	19
4	limit 3 to (human and yr="2000 -Current" and "review")	1

Embase search results

#	Searches	Results
1	(Amphet* or methamphet*).ti,ab. or exp amphetamine/ or exp methamphetamine/	61164
2	exp Injection site abscess/ or exp Skin Abscess/ or (skin and inject*).ti,ab.	40409
3	1 and 2	61
4	limit 3 to (human and yr="2000 -Current" and "review")	6

Review of individual papers

Embase search results

#	Searches	Results
1	(Amphet* or methamphet*).ti,ab. or exp amphetamine/ or exp methamphetamine/	61164
2	exp injection site abscess/ or exp skin abscess/	3828
3	(skin and inject*).ti,ab.	36713
4	2 or 3	40409
5	1 and 4	61
6	limit 5 to (human and yr="2000 -Current")	31

Cocaine

Review of reviews

Abscess or injection site irritation

Medline search results

#	Searches	Results
1	cocaine*.ti,ab. or exp Cocaine/ or exp cocaine dependence/ or exp cocaine derivative/	37171
2	exp Injection site abscess/ or exp Skin Abscess/ or (skin and inject*).ti,ab.	19445
3	1 and 2	56
4	limit 3 to (human and yr="2000 -Current" and 'review')	5

Embase search results

#	Searches	Results
1	cocaine*.ti,ab. or exp Cocaine/ or exp cocaine dependence/ or exp cocaine derivative/	63755
2	exp Injection site abscess/ or exp Skin Abscess/ or (skin and inject*).ti,ab.	40409
3	1 and 2	139
4	limit 3 to (human and yr="2000 -Current" and 'review')	16

Review of individual papers

Embase search results

#	Searches	Results
1	cocaine*.ti,ab. or exp Cocaine/ or exp cocaine dependence/ or exp cocaine derivative/	63755
2	Injection site abscess/ or Skin Abscess/ or (skin and inject*).ti,ab.	40409
3	1 and 2	139
4	limit 3 to (human and yr="2000 -Current")	79

HIV (sex risk)

Amphetamine-type stimulants

Review of reviews

Medline search results

#	Searches	Results
1	(Amphet* or methamphet*).ti,ab. or exp amphetamine/ or exp methamphetamine/	36981
2	(HIV adj3 sex).ti,ab. or (exp Human Immunodeficiency Virus/ and (exp Sexual Transmission/ or exp Sexual Behaviour/))	2098
3	1 and 2	38
4	limit 3 to (human and yr="2000 -Current" and "review")	1

Embase search results

#	Searches	Results
1	(Amphet* or methamphet*).ti,ab. or exp amphetamine/ or exp methamphetamine/	61164
2	(HIV adj3 sex).ti,ab. or (exp Human Immunodeficiency Virus/ and (exp Sexual Transmission/ or exp Sexual Behaviour/))	12261
3	1 and 2	213
4	limit 3 to (human and yr="2000 -Current" and "review")	19

Review of individual papers

Embase search results

#	Searches	Results
1	(Amphet* or methamphet*).ti,ab. or exp amphetamine/ or exp methamphetamine/	61164
2	(HIV adj3 sex).ti,ab.	2820
3	exp Human Immunodeficiency Virus/	172255
4	exp Sexual Transmission/ or exp Sexual Behaviour/	200049
5	3 and 4	9937
6	2 or 5	12261

#	Searches	Results
7	1 and 6	213
8	limit 7 to (human and yr="2000 -Current")	191

Cocaine

Review of reviews

Medline search results

#	Searches	Results
1	cocaine*.ti,ab. or exp Cocaine/ or exp cocaine dependence/ or exp cocaine derivative/	37171
2	(HIV adj3 sex).ti,ab. or (exp Human Immunodeficiency Virus/ and (exp Sexual Transmission/ or exp Sexual Behaviour/))	2093
3	1 and 2	68
4	limit 3 to (human and yr="2000 -Current" and 'review'	0

Embase search results

#	Searches	Results
1	cocaine*.ti,ab. or exp Cocaine/ or exp cocaine dependence/ or exp cocaine derivative/	63755
2	(HIV adj3 sex).ti,ab. or (exp Human Immunodeficiency Virus/ and (exp Sexual Transmission/ or exp Sexual Behaviour/))	12261
3	1 and 2	361
4	limit 3 to (human and yr="2000 -Current" and 'review'	16

Review of individual papers

Embase search results

#	Searches	Results
1	cocaine*.ti,ab. or exp Cocaine/ or exp cocaine dependence/ or exp cocaine derivative/	63755
2	(HIV adj3 sex).ti,ab. or (Human Immunodeficiency Virus/ and (Sexual Transmission/ or Sexual Behaviour/))	7250
3	1 and 2	257
4	limit 3 to (human and yr="2000 -Current")	205

HIV (injecting risk)

Amphetamine-type stimulants

Review of reviews

Medline search results

#	Searches	Results
1	(Amphet* or methamphet*).ti,ab. or exp amphetamine/ or exp methamphetamine/	36981
2	(HIV adj3 inject*).ti,ab. or (exp Human Immunideficiency Virus/ and (exp Intravenous Drug Abuse/ or inject*.ti,ab. or injecting risk.ti,ab.))	1712
3	1 and 2	45
4	limit 3 to (human and yr="2000 -Current" and "review")	2

Embase search results

#	Searches	Results
1	(Amphet* or methamphet*).ti,ab. or exp amphetamine/ or exp methamphetamine/	61164
2	(HIV adj3 inject*).ti,ab. or (exp Human Immunideficiency Virus/ and (exp Intravenous Drug Abuse/ or inject*.ti,ab. or injecting risk.ti,ab.))	2140
3	1 and 2	93
4	limit 3 to (human and yr="2000 -Current" and "review")	9

Review of individual papers

Embase search results

#	Searches	Results
1	(Amphet* or methamphet*).ti,ab. or exp amphetamine/ or exp methamphetamine/	61164
2	(HIV adj3 inject*).ti,ab. or (Human Immunideficiency Virus/ and (Intravenous Drug Abuse/ or inject*.ti,ab. or injecting risk.ti,ab.))	2140
3	1 and 2	93
4	limit 3 to (human and yr="2000 -Current")	69

Cocaine

Review of reviews

Medline search results

#	Searches	Results
1	cocaine*.ti,ab. or exp Cocaine/ or exp cocaine dependence/ or exp cocaine derivative/	37171
2	(HIV adj3 inject*).ti,ab. or (exp Human Immunideficiency Virus/ and (exp Intravenous Drug Abuse/ or inject*.ti,ab. or injecting risk.ti,ab.))	1711
3	1 and 2	126
4	limit 3 to (human and yr="2000 -Current" and 'review'	4

Embase search results

#	Searches	Results
1	cocaine*.ti,ab. or exp Cocaine/ or exp cocaine dependence/ or exp cocaine derivative/	63755
2	(HIV adj3 inject*).ti,ab. or (exp Human Immunideficiency Virus/ and (exp Intravenous Drug Abuse/ or inject*.ti,ab. or injecting risk.ti,ab.))	2140
3	1 and 2	233
4	limit 3 to (human and yr="2000 -Current" and 'review'	20

Review of individual papers

Embase search results

#	Searches	Results
1	cocaine*.ti,ab. or exp Cocaine/ or exp cocaine dependence/ or exp cocaine derivative/	63755
2	(HIV adj3 inject*).ti,ab. or (Human Immunideficiency Virus/ and (Intravenous Drug Abuse/ or inject*.ti,ab. or injecting risk.ti,ab.))	2140
3	1 and 2	233
4	limit 3 to (human and yr="2000 -Current")	169

HCV

Amphetamine-type stimulants

Review of reviews

Medline search results

#	Searches	Results
1	(Amphet* or methamphet*).ti,ab. or exp amphetamine/ or exp methamphetamine/	36981
2	exp Hepatitis C/ or "HCV".ti,ab.	68898
3	1 and 2	111
4	limit 3 to (human and yr="2000 -Current" and "review")	13

Embase search results

#	Searches	Results
1	(Amphet* or methamphet*).ti,ab. or exp amphetamine/ or exp methamphetamine/	61164
2	exp Hepatitis C/ or "HCV".ti,ab.	131240
3	1 and 2	474
4	limit 3 to (human and yr="2000 -Current" and "review")	52

Review of individual papers

Embase search results

#	Searches	Results
1	(Amphet* or methamphet*).ti,ab. or exp amphetamine/ or exp methamphetamine/	61164
2	exp hepatitis C/	98919
3	"HCV".ti,ab.	81744
4	2 or 3	131240
5	1 and 4	474
6	limit 5 to (human and yr="2000 -Current")	437

Cocaine

Review of reviews

Medline search results

#	Searches	Results
1	cocaine*.ti,ab. or exp Cocaine/ or exp cocaine dependence/ or exp cocaine derivative/	37171
2	exp Hepatitis C/ or "HCV".ti,ab.	68809
3	1 and 2	263
4	limit 3 to (human and yr="2000 -Current" and 'review'	20

Embase search results

#	Searches	Results
1	cocaine*.ti,ab. or exp Cocaine/ or exp cocaine dependence/ or exp cocaine derivative/	63755
2	exp Hepatitis C/ or "HCV".ti,ab.	131240
3	1 and 2	973
4	limit 3 to (human and yr="2000 -Current" and 'review'	97

Review of individual papers

Embase search results

#	Searches	Results
1	cocaine*.ti,ab. or exp Cocaine/ or exp cocaine dependence/ or exp cocaine derivative/	63755
2	Hepatitis C/ or "HCV".ti,ab.	129036
3	1 and 2	967
4	limit 3 to (human and yr="2000 -Current")	888

HBV

Amphetamine-type stimulants

Review of reviews

Medline search results

#	Searches	Results
1	(Amphet* or methamphet*).ti,ab. or exp amphetamine/ or exp methamphetamine/	36981
2	exp Hepatitis B/ or "HBV".ti,ab.	63147
3	1 and 2	45
4	limit 3 to (human and yr="2000 -Current" and "review")	1

Embase search results

#	Searches	Results
1	(Amphet* or methamphet*).ti,ab. or exp amphetamine/ or exp methamphetamine/	61164
2	exp Hepatitis B/ or "HBV".ti,ab.	113015
3	1 and 2	145
4	limit 3 to (human and yr="2000 -Current" and "review")	18

Review of individual papers

Embase search results

#	Searches	Results
1	(Amphet* or methamphet*).ti,ab. or exp amphetamine/ or exp methamphetamine/	61164
2	exp Hepatitis B/ or "HBV".ti,ab.	113015
3	1 and 2	145
4	limit 3 to (human and yr="2000 -Current")	112

Cocaine

Review of reviews

Medline search results

#	Searches	Results
1	cocaine*.ti,ab. or exp Cocaine/ or exp cocaine dependence/ or exp cocaine derivative/	37171
2	Hepatitis B/ or "HBV".ti,ab.	63096
3	1 and 2	87
4	limit 3 to (human and yr="2000 -Current" and 'review'	3

Embase search results

#	Searches	Results
1	cocaine*.ti,ab. or exp Cocaine/ or exp cocaine dependence/ or exp cocaine derivative/	63755
2	Hepatitis B/ or "HBV".ti,ab.	113015
3	1 and 2	318
4	limit 3 to (human and yr="2000 -Current" and 'review'	39

Review of individual papers

Embase search results

#	Searches	Results
1	cocaine*.ti,ab. or exp Cocaine/ or exp cocaine dependence/ or exp cocaine derivative/	63755
2	Hepatitis B/ or "HBV".ti,ab.	110487
3	1 and 2	316
4	limit 3 to (human and yr="2000 -Current")	271

Tuberculosis

Amphetamine-type stimulants

Review of reviews

Medline search results

#	Searches	Results
1	(Amphet* or methamphet*).ti,ab. or exp amphetamine/ or exp methamphetamine/	36981
2	exp Tuberculosis/ or Mycobacterium tuberculosis.ti,ab. or "TB".ti,ab.	207783
3	1 and 2	25
4	limit 3 to (human and yr="2000 -Current" and "review")	1

Embase search results

#	Searches	Results
1	(Amphet* or methamphet*).ti,ab. or exp amphetamine/ or exp methamphetamine/	61164
2	exp Tuberculosis/ or Mycobacterium tuberculosis.ti,ab. or "TB".ti,ab.	292693
3	1 and 2	87
4	limit 3 to (human and yr="2000 -Current" and "review")	14

Review of individual papers

Embase search results

#	Searches	Results
1	(Amphet* or methamphet*).ti,ab. or exp amphetamine/ or exp methamphetamine/	61164
2	exp Tuberculosis/ or Mycobacterium tuberculosis.ti,ab. or "TB".ti,ab.	292693
3	1 and 2	87
4	limit 3 to (human and yr="2000 -Current")	59

Cocaine

Review of reviews

Medline search results

#	Searches	Results
1	cocaine*.ti,ab. or exp Cocaine/ or exp cocaine dependence/ or exp cocaine derivative/	37171
2	exp Tuberculosis/ or Mycobacterium tuberculosis.ti,ab. or "TB".ti,ab.	207538
3	1 and 2	61
4	limit 3 to (human and yr="2000 -Current" and 'review'	3

Embase search results

#	Searches	Results
1	cocaine*.ti,ab. or exp Cocaine/ or exp cocaine dependence/ or exp cocaine derivative/	63755
2	exp Tuberculosis/ or Mycobacterium tuberculosis.ti,ab. or "TB".ti,ab.	292693
3	1 and 2	240
4	limit 3 to (human and yr="2000 -Current" and 'review'	36

Review of individual papers

Embase search results

#	Searches	Results
1	cocaine*.ti,ab. or exp Cocaine/ or exp cocaine dependence/ or exp cocaine derivative/	63755
2	Tuberculosis/ or Mycobacterium tuberculosis.ti,ab. or "TB".ti,ab.	214941
3	1 and 2	202
4	limit 3 to (human and yr="2000 -Current")	137

Other sexually transmitted diseases

Amphetamine-type stimulants

Review of reviews

Medline search results

#	Searches	Results
1	(Amphet* or methamphet*).ti,ab. or exp amphetamine/ or exp methamphetamine/	36981
2	exp Sexually Transmitted Disease/ or (sexua* adj3 disease).ti,ab. or (sexua* adj3 infect*).ti,ab. or "STI".ti,ab. or "STD".ti,ab.	323170
3	1 and 2	871
4	limit 3 to (human and yr="2000 -Current" and "review")	73

Embase search results

#	Searches	Results
1	(Amphet* or methamphet*).ti,ab. or exp amphetamine/ or exp methamphetamine/	61164
2	exp Sexually Transmitted Disease/ or (sexua* adj3 disease).ti,ab. or (sexua* adj3 infect*).ti,ab. or "STI".ti,ab. or "STD".ti,ab.	120251
3	1 and 2	528

4	limit 3 to (human and yr="2000 -Current" and "review")	51

Review of individual papers

Embase search results

#	Searches	Results
1	(Amphet* or methamphet*).ti,ab. or exp amphetamine/ or exp methamphetamine/	61164
2	exp Sexually Transmitted Disease/ or (sexua* adj3 disease).ti,ab. or (sexua* adj3 infect*).ti,ab. or "STI".ti,ab. or "STD".ti,ab.	120251
3	1 and 2	528
4	limit 3 to (human and yr="2000 -Current")	458

Cocaine

Review of reviews

Medline search results

#	Searches	Results
1	cocaine*.ti,ab. or exp Cocaine/ or exp cocaine dependence/ or exp cocaine derivative/	37171
2	exp Sexually Transmitted Disease/ OR ((sexua* adj3 disease).ti,ab) OR ((sexua* adj3 infect*).ti,ab) OR "STI".ti,ab OR "STD".ti,ab	322922
3	1 and 2	1854
4	limit 3 to (human and yr="2000 -Current" and 'review'	76

Embase search results

#	Searches	Results
1	cocaine*.ti,ab. or exp Cocaine/ or exp cocaine dependence/ or exp cocaine derivative/	63755
2	exp Sexually Transmitted Disease/ OR ((sexua* adj3 disease).ti,ab) OR ((sexua* adj3 infect*).ti,ab) OR "STI".ti,ab OR "STD".ti,ab	120251
3	1 and 2	869
4	limit 3 to (human and yr="2000 -Current" and 'review'	74

Review of individual papers

Embase search results

#	Searches	Results
1	cocaine*.ti,ab. or exp Cocaine/ or exp cocaine dependence/ or exp cocaine derivative/	63755
2	Sexually Transmitted Disease/ or (sexua* adj3 disease).ti,ab. or (sexua* adj3 infect*).ti,ab. or "STI".ti,ab. or "STD".ti,ab.	64398
3	1 and 2	690
4	limit 3 to (human and yr="2000 -Current")	504

Neonatal outcomes

Amphetamine-type stimulants

Review of reviews

Preterm birth

Medline search results

#	Searches	Results
1	(Amphet* or methamphet*).ti,ab. or exp amphetamine/ or exp methamphetamine/	36981
2	exp Premature labor/ or exp Prematurity/	22758
3	1 and 2	6
4	limit 3 to (human and yr="2000 -Current" and "review")	0

Embase search results

#	Searches	Results
1	(Amphet* or methamphet*).ti,ab. or exp amphetamine/ or exp methamphetamine/	61164
2	exp Premature labor/ or exp Prematurity/	135068
3	1 and 2	120
4	limit 3 to (human and yr="2000 -Current" and "review")	27

Low birth weight

Medline search results

#	Searches	Results
1	(Amphet* or methamphet*).ti,ab. or exp amphetamine/ or exp methamphetamine/	36981
2	exp Birth Weight/	38041
3	1 and 2	40
4	limit 3 to (human and yr="2000 -Current" and "review")	1

Embase search results

#	Searches	Results
1	(Amphet* or methamphet*).ti,ab. or exp amphetamine/ or exp methamphetamine/	61164
2	exp Birth Weight/	108354
3	1 and 2	154
4	limit 3 to (human and yr="2000 -Current" and "review")	29

Congenital abnormalities

Medline search results

#	Searches	Results
1	(Amphet* or methamphet*).ti,ab. or exp amphetamine/ or exp methamphetamine/	36981
2	exp Newborn Disease/ or exp Apgar Score/ or exp Congenital disorder/ or neonat*.ti,ab.	1270352
3	1 and 2	745
4	limit 3 to (human and yr="2000 -Current" and "review")	31

Embase search results

#	Searches	Results
1	(Amphet* or methamphet*).ti,ab. or exp amphetamine/ or exp methamphetamine/	61164

2	exp Newborn Disease/ or exp Apgar Score/ or exp Congenital disorder/ or neonat*.ti,ab.	1725093
3	1 and 2	1585
4	limit 3 to (human and yr="2000 -Current" and "review")	245

Review of individual papers

Embase search results

#	Searches	Results
1	(amphet$ or methamphet$).ti,ab. or exp amphetamine/ or exp methamphetamine/	61180
2	exp Premature labor/ or exp Prematurity/	135117
3	exp Birth Weight/	108391
4	exp Newborn Disease/ or exp Apgar Score/ or exp Congenital disorder/ or neonat*.ti,ab.	1725856
5	2 or 3 or 4	1770366
6	1 and 5	1620
7	limit 6 to (human and yr="2000 -Current")	789

Note: Due to search being run on a different day to the other searches, result numbers slightly different

Cocaine

Review of reviews

Preterm birth

Medline search results

#	Searches	Results
1	Cocaine$.ti,ab. or exp Cocaine/ or exp cocaine dependence/ or exp cocaine derivative/	37171
2	exp Premature labor/ or exp Prematurity/	22742
3	1 and 2	46
4	limit 3 to (human and yr="2000 -Current" and 'review')	4

Embase search results

#	Searches	Results
1	Cocaine$.ti,ab. or exp Cocaine/ or exp cocaine dependence/ or exp cocaine derivative/	63755
2	exp Premature labor/ or exp Prematurity/	135068
3	1 and 2	347
4	limit 3 to (human and yr="2000 -Current" and 'review')	61

Low birth weight

Medline search results

#	Searches	Results
1	Cocaine$.ti,ab. or exp Cocaine/ or exp cocaine dependence/ or exp cocaine derivative/	37171
2	exp Birth Weight/	38018
3	1 and 2	144
4	limit 3 to (human and yr="2000 -Current" and 'review')	5

Embase search results

#	Searches	Results
1	Cocaine$.ti,ab. or exp Cocaine/ or exp cocaine dependence/ or exp cocaine derivative/	63755
2	exp Birth Weight/	108354
3	1 and 2	403
4	limit 3 to (human and yr="2000 -Current" and 'review')	39

Congenital abnormalities

Medline search results

#	Searches	Results
1	Cocaine$.ti,ab. or exp Cocaine/ or exp cocaine dependence/ or exp cocaine derivative/	37171
2	exp Newborn Disease/ OR exp Apgar Score/ Or exp Congenital disorder/ OR neonat*.ti,ab.	1269597
3	1 and 2	1254
4	limit 3 to (human and yr="2000 -Current" and 'review')	93

Embase search results

#	Searches	Results
1	Cocaine$.ti,ab. or exp Cocaine/ or exp cocaine dependence/ or exp cocaine derivative/	63755
2	exp Newborn Disease/ OR exp Apgar Score/ Or exp Congenital disorder/ OR neonat*.ti,ab.	1725093
3	1 and 2	2361
4	limit 3 to (human and yr="2000 -Current" and 'review')	382

Review of individual papers

Embase search results

#	Searches	Results
1	Cocaine$.ti,ab. or exp Cocaine/ or exp cocaine dependence/ or exp cocaine derivative/	63773
2	exp Premature labor/ or exp Prematurity/	135117
3	exp Birth Weight/	108391
4	exp Newborn Disease/ or exp Apgar Score/ or exp Congenital disorder/ or neonat*.ti,ab.	1725856
5	2 or 3 or 4	1770366
6	1 and 5	2490
7	limit 6 to (human and yr="2000 -Current")	1344

Note: Due to search being run on a different day to the other searches, result numbers slightly differ

Diseases of the nervous system

Amphetamine-type stimulants

Review of reviews

Parkinson's disease

Medline search results

#	Searches	Results
1	(Amphet* or methamphet*).ti,ab. or exp amphetamine/ or exp methamphetamine/	36981

2	exp Parkinson Disease/ or parkinson* disease.ti,ab.	78837
3	1 and 2	994
4	limit 3 to (human and yr="2000 -Current" and "review")	93

Embase search results

#	Searches	Results
1	(Amphet* or methamphet*).ti,ab. or exp amphetamine/ or exp methamphetamine/	61164
2	exp Parkinson Disease/ or parkinson* disease.ti,ab.	147423
3	1 and 2	1938
4	limit 3 to (human and yr="2000 -Current" and "review")	321

Epilepsy

Medline search results

#	Searches	Results
1	(Amphet* or methamphet*).ti,ab. or exp amphetamine/ or exp methamphetamine/	36981
2	exp Epilepsy/ or epileps*.ti,ab.	120098
3	1 and 2	177
4	limit 3 to (human and yr="2000 -Current" and "review")	12

Embase search results

#	Searches	Results
1	(Amphet* or methamphet*).ti,ab. or exp amphetamine/ or exp methamphetamine/	61164
2	exp Epilepsy/ or epileps*.ti,ab.	244841
3	1 and 2	822
4	limit 3 to (human and yr="2000 -Current" and "review")	177

Dyskinesia

Medline search results

#	Searches	Results
1	(Amphet* or methamphet*).ti,ab. or exp amphetamine/ or exp methamphetamine/	36981
2	exp Dyskinesia/ or exp Motor Dysfunction/	73726
3	1 and 2	1266
4	limit 3 to (human and yr="2000 -Current" and "review")	19

Embase search results

#	Searches	Results
1	(Amphet* or methamphet*).ti,ab. or exp amphetamine/ or exp methamphetamine/	61164
2	exp Dyskinesia/ or exp Motor Dysfunction/	734284
3	1 and 2	4959
4	limit 3 to (human and yr="2000 -Current" and "review")	931

Sleep disorders

Medline search results

#	Searches	Results
1	(Amphet* or methamphet*).ti,ab. or exp amphetamine/ or exp methamphetamine/	36981
2	exp Sleep Disorder/ or sleep* problem.ti,ab. or sleep* disord*.ti,ab.	79230
3	1 and 2	387
4	limit 3 to (human and yr="2000 -Current" and "review")	53

Embase search results

#	Searches	Results
1	(Amphet* or methamphet*).ti,ab. or exp amphetamine/ or exp methamphetamine/	61164
2	exp Sleep Disorder/ or sleep* problem.ti,ab. or sleep* disord*.ti,ab.	203206
3	1 and 2	2577
4	limit 3 to (human and yr="2000 -Current" and "review")	918

Neurotoxic effects

Medline search results

#	Searches	Results
1	(Amphet* or methamphet*).ti,ab. or exp amphetamine/ or exp methamphetamine/	36981
2	exp Neurotoxicity/ or (toxi* adj3 neuro*).ti,ab.	9316
3	1 and 2	127
4	limit 3 to (human and yr="2000 -Current" and "review")	11

Embase search results

#	Searches	Results
1	(Amphet* or methamphet*).ti,ab. or exp amphetamine/ or exp methamphetamine/	61164
2	exp Neurotoxicity/ or (toxi* adj3 neuro*).ti,ab.	100780
3	1 and 2	2488
4	limit 3 to (human and yr="2000 -Current" and "review")	313

Review of individual papers

Embase search results

#	Searches	Results
1	(Amphet* or methamphet*).ti,ab. or exp amphetamine/ or exp methamphetamine/	61164
2	exp Parkinson Disease/ or parkinson* disease.ti,ab.	147423
3	exp Epilepsy/ or epileps*.ti,ab.	244841
4	Dyskinesia/ or Motor Dysfunction/	75141
5	Sleep Disorder/ or sleep* problem.ti,ab. or sleep* disord*.ti,ab.	69727
6	Neurotoxicity/ or (toxi* adj3 neuro*).ti,ab.	100780
7	2 or 3 or 4 or 5 or 6	584782
8	1 and 7	5828
9	limit 8 to (human and yr="2008 -Current")	1428

Cocaine

Review of reviews

Parkinson's disease

Medline search results

#	Searches	Results
1	cocaine*.ti,ab. or exp Cocaine/ or exp cocaine dependence/ or exp cocaine derivative/	37171
2	exp Parkinson Disease/ or parkinson* disease.ti,ab.	78690
3	1 and 2	374
4	limit 3 to (human and yr="2000 -Current" and 'review'	54

Embase search results

#	Searches	Results
1	cocaine*.ti,ab. or exp Cocaine/ or exp cocaine dependence/ or exp cocaine derivative/	63755
2	exp Parkinson Disease/ or parkinson* disease.ti,ab.	147423
3	1 and 2	644
4	limit 3 to (human and yr="2000 -Current" and 'review'	207

Epilepsy

Medline search results

#	Searches	Results
1	cocaine*.ti,ab. or exp Cocaine/ or exp cocaine dependence/ or exp cocaine derivative/	37171
2	exp Parkinson Disease/ or parkinson* disease.ti,ab.	119968
3	1 and 2	99
4	limit 3 to (human and yr="2000 -Current" and 'review'	14

Embase search results

#	Searches	Results
1	cocaine*.ti,ab. or exp Cocaine/ or exp cocaine dependence/ or exp cocaine derivative/	63755
2	exp Parkinson Disease/ or parkinson* disease.ti,ab.	244841
3	1 and 2	624
4	limit 3 to (human and yr="2000 -Current" and 'review'	168

Dyskinesia

Medline search results

#	Searches	Results
1	cocaine*.ti,ab. or exp Cocaine/ or exp cocaine dependence/ or exp cocaine derivative/	37171
2	exp Dyskinesia/ or exp Motor Dysfunction/	73678
3	1 and 2	326
4	limit 3 to (human and yr="2000 -Current" and 'review'	12

Embase search results

#	Searches	Results

1	cocaine*.ti,ab. or exp Cocaine/ or exp cocaine dependence/ or exp cocaine derivative/	63755
2	exp Dyskinesia/ or exp Motor Dysfunction/	734284
3	1 and 2	2616
4	limit 3 to (human and yr="2000 -Current" and 'review'	557

Sleep disorders

Medline search results

#	Searches	Results
1	cocaine*.ti,ab. or exp Cocaine/ or exp cocaine dependence/ or exp cocaine derivative/	37171
2	exp Sleep Disorder/ OR (sleep* problem).ti,ab OR (sleep* disord*).ti,ab	79159
3	1 and 2	131
4	limit 3 to (human and yr="2000 -Current" and 'review'	17

Embase search results

#	Searches	Results
1	cocaine*.ti,ab. or exp Cocaine/ or exp cocaine dependence/ or exp cocaine derivative/	63755
2	exp Sleep Disorder/ OR (sleep* problem).ti,ab OR (sleep* disord*).ti,ab	203206
3	1 and 2	1068
4	limit 3 to (human and yr="2000 -Current" and 'review'	366

Neurotoxic effects

Medline search results

#	Searches	Results
1	cocaine*.ti,ab. or exp Cocaine/ or exp cocaine dependence/ or exp cocaine derivative/	37171
2	exp Neurotoxicity/ OR (toxi* adj3 neuro*).ti,ab	9312
3	1 and 2	43
4	limit 3 to (human and yr="2000 -Current" and 'review'	11

Embase search results

#	Searches	Results
1	cocaine*.ti,ab. or exp Cocaine/ or exp cocaine dependence/ or exp cocaine derivative/	63755
2	exp Neurotoxicity/ OR (toxi* adj3 neuro*).ti,ab	100780
3	1 and 2	930
4	limit 3 to (human and yr="2000 -Current" and 'review'	213

Review of individual papers

Embase search results

#	Searches	Results
1	cocaine*.ti,ab. or exp Cocaine/ or exp cocaine dependence/ or exp cocaine derivative/	63755
2	Parkinson Disease/ or parkinson* disease.ti,ab.	147388
3	Epilepsy/ or epileps*.ti,ab.	187779
4	Dyskinesia/ or Motor Dysfunction/	75141

#	Searches	Results
5	Sleep Disorder/ or sleep* problem.ti,ab. or sleep* disord*.ti,ab.	69727
6	Neurotoxicity/ or (toxi* adj3 neuro*).ti,ab.	100780
7	2 or 3 or 4 or 5 or 6	532638
8	1 and 7	2277
9	limit 8 to (human and yr="2000 -Current")	1345

Criminal involvement

Amphetamine-type stimulants

Review of reviews

Medline search results

#	Searches	Results
1	(Amphet* or methamphet*).ti,ab. or exp amphetamine/ or exp methamphetamine/	36981
2	exp Offender/ or crim*.ti,ab. or (crim* adj3 behavi*).ti,ab. or (crim* adj3 act*).ti,ab.	30316
3	1 and 2	275
4	limit 3 to (human and yr="2000 -Current" and "review")	30

Embase search results

#	Searches	Results
1	(Amphet* or methamphet*).ti,ab. or exp amphetamine/ or exp methamphetamine/	61164
2	exp Offender/ or crim*.ti,ab. or (crim* adj3 behavi*).ti,ab. or (crim* adj3 act*).ti,ab.	50199
3	1 and 2	640
4	limit 3 to (human and yr="2000 -Current" and "review")	60

Review of individual papers

Embase search results

#	Searches	Results
1	(Amphet* or methamphet*).ti,ab. or exp amphetamine/ or exp methamphetamine/	61164
2	Offender/ or crim*.ti,ab. or (crim* adj3 behavi*).ti,ab. or (crim* adj3 act*).ti,ab.	50199
3	1 and 2	640
4	limit 3 to (human and yr="2000 -Current")	475

Cocaine

Review of reviews

Medline search results

#	Searches	Results
1	cocaine*.ti,ab. or exp Cocaine/ or exp cocaine dependence/ or exp cocaine derivative/	37171

2	exp Offender/ or crim*.ti,ab. or (crim* adj3 behavi*).ti,ab. or (crim* adj3 act*).ti,ab.	30270
3	1 and 2	504
4	limit 3 to (human and yr="2000 -Current" and 'review'	38

Embase search results

#	Searches	Results
1	cocaine*.ti,ab. or exp Cocaine/ or exp cocaine dependence/ or exp cocaine derivative/	63755
2	exp Offender/ or crim*.ti,ab. or (crim* adj3 behavi*).ti,ab. or (crim* adj3 act*).ti,ab.	50199
3	1 and 2	1050
4	limit 3 to (human and yr="2000 -Current" and 'review'	92

Review of individual papers

Embase search results

#	Searches	Results
1	cocaine*.ti,ab. or exp Cocaine/ or exp cocaine dependence/ or exp cocaine derivative/	63755
2	Offender/ or crim*.ti,ab. or (crim* adj3 behavi*).ti,ab. or (crim* adj3 act*).ti,ab.	50199
3	1 and 2	1050
4	limit 3 to (human and yr="2000 -Current")	695

Suicide

Amphetamine-type stimulants

Review of reviews

Medline search results

#	Searches	Results
1	(Amphet* or methamphet*).ti,ab. or exp amphetamine/ or exp methamphetamine/	36981
2	exp Suicide/ or exp Suicide Attempt/ or suicid*.ti,ab.	74970
3	1 and 2	263
4	limit 3 to (human and yr="2000 -Current" and "review")	17

Embase search results

#	Searches	Results
1	(Amphet* or methamphet*).ti,ab. or exp amphetamine/ or exp methamphetamine/	61164
2	exp Suicide/ or exp Suicide Attempt/ or suicid*.ti,ab.	106352
3	1 and 2	744
4	limit 3 to (human and yr="2000 -Current" and "review")	109

Review of individual papers

Embase search results

#	Searches	Results
1	(Amphet* or methamphet*).ti,ab. or exp amphetamine/ or exp methamphetamine/	61164

2	Suicide/ or Suicide Attempt/ or suicid*.ti,ab.	106352
3	1 and 2	744
4	limit 3 to (human and yr="2000 -Current")	551

Cocaine

Review of reviews

Medline search results

#	Searches	Results
1	cocaine*.ti,ab. or exp Cocaine/ or exp cocaine dependence/ or exp cocaine derivative/	37171
2	exp Suicide/ or exp Suicide Attempt/ or suicid*.ti,ab.	74904
3	1 and 2	390
4	limit 3 to (human and yr="2000 -Current" and 'review'	20

Embase search results

#	Searches	Results
1	cocaine*.ti,ab. or exp Cocaine/ or exp cocaine dependence/ or exp cocaine derivative/	63755
2	exp Suicide/ or exp Suicide Attempt/ or suicid*.ti,ab.	106352
3	1 and 2	942
4	limit 3 to (human and yr="2000 -Current" and 'review'	113

Review of individual papers

Embase search results

#	Searches	Results
1	cocaine*.ti,ab. or exp Cocaine/ or exp cocaine dependence/ or exp cocaine derivative/	63755
2	Suicide/ or Suicide Attempt/ or suicid*.ti,ab.	106352
3	1 and 2	942
4	limit 3 to (human and yr="2000 -Current")	703

Self-harm

Amphetamine-type stimulants

Review of reviews

Medline search results

#	Searches	Results
1	(Amphet* or methamphet*).ti,ab. or exp amphetamine/ or exp methamphetamine/	36981
2	exp Automutilation/ or self harm*.ti,ab. or (injur* adj3 self*).ti,ab. or (harm* adj3 self*).ti,ab.	8341
3	1 and 2	59
4	limit 3 to (human and yr="2000 -Current" and "review")	5

Embase search results

#	Searches	Results
1	(Amphet* or methamphet*).ti,ab. or exp amphetamine/ or exp methamphetamine/	61164

2	exp Automutilation/ or self harm*.ti,ab. or (injur* adj3 self*).ti,ab. or (harm* adj3 self*).ti,ab.	20531
3	1 and 2	209
4	limit 3 to (human and yr="2000 -Current" and "review")	29

Review of individual papers

Embase search results

#	Searches	Results
1	(Amphet* or methamphet*).ti,ab. or exp amphetamine/ or exp methamphetamine/	61164
2	Automutilation/ or self harm*.ti,ab. or (injur* adj3 self*).ti,ab. or (harm* adj3 self*).ti,ab.	20531
3	1 and 2	209
4	limit 3 to (human and yr="2000 -Current")	147

Cocaine

Review of reviews

Medline search results

#	Searches	Results
1	cocaine*.ti,ab. or exp Cocaine/ or exp cocaine dependence/ or exp cocaine derivative/	37171
2	exp Automutilation/ or self harm*.ti,ab. or (injur* adj3 self*).ti,ab. or (harm* adj3 self*).ti,ab.	8323
3	1 and 2	38
4	limit 3 to (human and yr="2000 -Current" and 'review'	4

Embase search results

#	Searches	Results
1	cocaine*.ti,ab. or exp Cocaine/ or exp cocaine dependence/ or exp cocaine derivative/	63755
2	exp Automutilation/ or self harm*.ti,ab. or (injur* adj3 self*).ti,ab. or (harm* adj3 self*).ti,ab.	20531
3	1 and 2	163
4	limit 3 to (human and yr="2000 -Current" and 'review'	22

Review of individual papers

Embase search results

#	Searches	Results
1	cocaine*.ti,ab. or exp Cocaine/ or exp cocaine dependence/ or exp cocaine derivative/	63755
2	Automutilation/ or self harm*.ti,ab. or (injur* adj3 self*).ti,ab. or (harm* adj3 self*).ti,ab.	20531
3	1 and 2	163
4	limit 3 to (human and yr="2000 -Current")	136

Violence

Amphetamine-type stimulants

Review of reviews

Medline search results

#	Searches	Results
1	(Amphet* or methamphet*).ti,ab. or exp amphetamine/ or exp methamphetamine/	36981
2	Violence/ or violen*.ti,ab. or (violen* adj3 behavi*).ti,ab. or exp Hostility/ or hosti*.ti,ab. or (hosti* adj3 behavi*).ti,ab. or exp Antisocial Behavior/	66055
3	1 and 2	255
4	limit 3 to (human and yr="2000 -Current" and "review")	19

Embase search results

#	Searches	Results
1	(Amphet* or methamphet*).ti,ab. or exp amphetamine/ or exp methamphetamine/	61164
2	exp Violence/ or violen*.ti,ab. or (violen* adj3 behavi*).ti,ab. or exp Hostility/ or hosti*.ti,ab. or (hosti* adj3 behavi*).ti,ab. or exp Antisocial Behavior/	199500
3	1 and 2	1211
4	limit 3 to (human and yr="2000 -Current" and "review")	174

Review of individual papers

Embase search results

#	Searches	Results
1	(Amphet* or methamphet*).ti,ab. or exp amphetamine/ or exp methamphetamine/	61164
2	Violence/ or violen*.ti,ab. or (violen* adj3 behavi*).ti,ab. or Hostility/ or hosti*.ti,ab. or (hosti* adj3 behavi*).ti,ab. or Antisocial Behavior/	102996
3	1 and 2	714
4	limit 3 to (human and yr="2000 -Current")	539

Cocaine

Review of reviews

Medline search results

#	Searches	Results
1	cocaine*.ti,ab. or exp Cocaine/ or exp cocaine dependence/ or exp cocaine derivative/	37171
2	exp Violence/ or violen*.ti,ab. or (violen* adj3 behavi*).ti,ab. or exp Hostility/ or hosti*.ti,ab. or (hosti* adj3 behavi*).ti,ab. or exp Antisocial Behavior/	110930
3	1 and 2	673
4	limit 3 to (human and yr="2000 -Current" and 'review'	39

Embase search results

#	Searches	Results
1	cocaine*.ti,ab. or exp Cocaine/ or exp cocaine dependence/ or exp cocaine derivative/	63755

2	exp Violence/ or violen*.ti,ab. or (violen* adj3 behavi*).ti,ab. or exp Hostility/ or hosti*.ti,ab. or (hosti* adj3 behavi*).ti,ab. or exp Antisocial Behavior/	199500
3	1 and 2	2211
4	limit 3 to (human and yr="2000 -Current" and 'review'	209

Review of individual papers

Embase search results

#	Searches	Results
1	cocaine*.ti,ab. or exp Cocaine/ or exp cocaine dependence/ or exp cocaine derivative/	63755
2	Violence/ or violen*.ti,ab. or (violen* adj3 behavi*).ti,ab. or Hostility/ or hosti*.ti,ab. or (hosti* adj3 behavi*).ti,ab. or Antisocial Behavior/	102996
3	1 and 2	1271
4	limit 3 to (human and yr="2000 -Current")	873

Elevated mortality risk

Amphetamine-type stimulants

Review of reviews

Medline search results

#	Searches	Results
1	(Amphet* or methamphet*).ti,ab. or exp amphetamine/ or exp methamphetamine/	36981
2	(mortal* or fatal* or death*).ti,ab. or exp death/ or exp "cause of death"/ or exp accidental death/ or exp mortality/ or exp sudden death/ or exp fatality/ or exp hospitalization/	1523004
3	1 and 2	1687
4	limit 3 to (human and yr="2000 -Current" and "review")	181

Embase search results

#	Searches	Results
1	(Amphet* or methamphet*).ti,ab. or exp amphetamine/ or exp methamphetamine/	61164
2	(mortal* or fatal* or death*).ti,ab. or exp death/ or exp "cause of death"/ or exp accidental death/ or exp mortality/ or exp sudden death/ or exp fatality/ or exp hospitalization/	2546978
3	1 and 2	3848
4	limit 3 to (human and yr="2000 -Current" and "review")	552

Review of individual papers

Embase search results

#	Searches	Results
1	(Amphet* or methamphet*).ti,ab. or exp amphetamine/ or exp methamphetamine/	61164
2	(mortal* or fatal* or death*).ti,ab. or exp death/ or exp "cause of death"/ or exp accidental death/ or exp mortality/ or exp sudden death/ or exp fatality/ or exp hospitalization/	2546978
3	1 and 2	3848
4	limit 3 to (human and yr="2000 -Current")	2465

Cocaine

Review of reviews

Medline search results

#	Searches	Results
1	cocaine*.ti,ab. or exp Cocaine/ or exp cocaine dependence/ or exp cocaine derivative/	37171
2	(mortal* or fatal* or death*).ti,ab. or exp death/ or exp "cause of death"/ or exp accidental death/ or exp mortality/ or exp sudden death/ or exp fatality/ or exp hospitalization/	1521282
3	1 and 2	2529
4	limit 3 to (human and yr="2000 -Current" and 'review'	203

Embase search results

#	Searches	Results
1	cocaine*.ti,ab. or exp Cocaine/ or exp cocaine dependence/ or exp cocaine derivative/	63755
2	(mortal* or fatal* or death*).ti,ab. or exp death/ or exp "cause of death"/ or exp accidental death/ or exp mortality/ or exp sudden death/ or exp fatality/ or exp hospitalization/	2546978
3	1 and 2	5366
4	limit 3 to (human and yr="2000 -Current" and 'review'	718

Review of individual papers

Embase search results

#	Searches	Results
1	cocaine*.ti,ab. or exp Cocaine/ or exp cocaine dependence/ or exp cocaine derivative/	63755
2	(mortal* or fatal* or death*).ti,ab. or exp death/ or exp "cause of death"/ or exp accidental death/ or exp mortality/ or exp sudden death/ or exp fatality/ or exp hospitalization/	2546978
3	1 and 2	5366
4	limit 3 to (human and yr="2000 -Current")	3528

Table I1: Evidence for potential causal impacts of amphetamine and cocaine use on a range of non-fatal health harms

	Amphetamines				Cocaine			
	Effect	**Level**	**Size of effect**	**Refs**	**Effect**	**Level**	**Size of effect**	**Refs**
Substance use								
Dependence (lifetime risk %)	↑	B	Lifetime cumulative probability: 11.2%	129	↑	B	Lifetime cumulative probability: : 15.6%	130
Non-fatal overdose/poisoning	↑	C	n/a	67	↑	C	n/a	131
Mental health								
Depression	↑	D	OR 1.6 (1.1 – 2.2)[a]	132	↑	B	OR 1.9 (0.9 – 4.0)	133
Anxiety	?	D	n/a	132	✗	B	OR 1.12 (0.8 – 1.8)	133
Psychosis	↑	E	OR 2.0 (1.3 – 3.3)[a]	132	↑	C	Cocaine-induced psychosis: 6.9-75.0%	134
Violence	↑	D	OR 2.2 (1.2 – 4.1)[a]	132	↑	?	No estimate available [b]	133
Physical Health								
Stroke / Myocardial infarction	↑	C	n/a	135	↑	C	aOR: 13.9 (1.48 to 9.4)	136
Respiratory/lung disease	↑	C	**n/a**	**137**	↑	C	Hospitalisations for asthma	133
Skin and soft tissue infection	↑	B	Current: 6.1 - 32.0%[PWID] Past 6-12 months: 6.9 – 37.7%[PWID] Lifetime: 6.2 – 68.6%[PWID]	**138**	↑	B	Current: 6.1 - 32.0%[PWID] Past 6-12 months: 6.9 – 37.7%[PWID] Lifetime: 6.2 – 68.6%[PWID]	138
Bloodborne viruses and STIs								
HIV	↑ ↑ ↑	B C B	OR 2.73 (2.16 to 3.46) MSM HR 3.43 (2.98-3.95) PWID: IRR 3.0 (2.2-4.1)	24,67 24 54	↑ ✗ ↑	B B B	Female sex workers: OR 3.89 (2.14 – 7.08) MSM: OR 1.49 (0.44 – 5.01) PWID: IRR 3.6 (2.8-4.7)	133 133 54
Hepatitis C virus (HCV)	↑ ✗	C, D	PWID: OR 2.43 (1.33–4.43) Non-PWID: OR 0.68 (0.38–1.23)	139 140,141	↑	B	OR 2.92 (2.50 – 3.40)	133
Sexually transmitted infections	?	C	n/a	142-145	↑	B	OR 2.59 (1.54 – 4.53)	133
Other harms								
Non-fatal Injury	↑	B	Injury: OR 6.19 (3.46 to 11.06)	146	↑?	B	Injury: OR 1.66 (0.91 to 3.02)	146
Neonatal outcomes	↑	B	Premature birth: OR 4.11 (3.05 - 5.55) Low birth weight: OR 3.29 (1.97 – 5.47) Small for gestational age: OR 5.79 (1.39–24.06)	**147**	↑	B	Foetal growth restriction: OR 2.30 (1.91 -2.78) Premature: OR 1.82 (1.01 – 3.27)	133
Parkinson's disease	↑	C	n/a	148	?			

[a] Any use versus no use of amphetamine or methamphetamine. No use could include the use of other substances.

[b] Increased for injecting cocaine use; results for other cocaine use not consistent

Level of evidence

A Experimental or controlled evidence supports this finding

B Findings across cohorts, representative, population-based
C Findings across cohorts of drug users
D Findings across cross-sectional studies, representative population-based, or case-control studies
E Cross-sectional associations among non-representative samples of drug users, case series suggesting outcomes

Webappendix J: Details of literature search on reviews of interventions to reduce other health outcomes

Description of Method

We used a multi-stage hierarchical searching process to identify sources reporting on the the impact of various interventions on health outcomes associated with amphetamine and cocaine use amongst samples who report use of these substances.

The intent was to search for and identify the highest quality study type (see Table 1) for each intervention and the associated health outcome.

Table 1. Classification system used in assessment of study methodologies

Level	Study type
1	Systematic review of all relevant randomised controlled trials
2	Properly designed randomised controlled trial
3.1	Well-designed pseudorandomised controlled trials [alternate allocation or some other method]
3.2	Comparative studies with concurrent controls and allocation not randomised [cohort studies], case-control studies, or interrupted time series with a control group
4	Case series, pre–test, and post–test, cross-sectional

There were four stages to searching, with stages 2-4 only undertaken if the highest level study type (i.e., level 1: systematic review of randomised controlled trials) was not identified in the previous stage. The hierarchy for selection of studies is detailed in Table 1. It should be noted that where narrative reviews were identified in stage 1 and 2, reference lists were searched for high-quality studies. Exclude study type 4.

Table 2. Hierarchy of searching for studies

Stage	Details
1	Cochrane Library of Systematic Reviews and EBM reviews search for Level 1 studies
2	Peer-reviewed literature database (Medline, Embase, PsycINFO) search for Level 1 studies
3	Peer-reviewed literature database (Medline, Embase, PsycINFO) search for Level 2-4 studies

Search Strategy

Cochrane Library of Systematic Reviews and EBM reviews (Full Text-Cochrane DSR, ACP Journal Club and DARE) search for Level 1 studies

The following searches were limited to those references published since 2000 and only Cochrane and CRD reviews

Cochrane Library

	Search Group	Number of citations retrieved
1	amphetamine OR amphetamines OR amphetamine-like	1630
2	Limit 1 to "Cochrane reviews" and “2000 – 2018”	22

	Search Group	Number of citations retrieved

1	cocaine	2661
2	Limit 1 to "Cochrane reviews" and “2000 – 2018”	23

EBM

	Search Group	Number of citations retrieved
1	amphetamine.mp. [mp=title, short title, abstract, full text, keywords, caption text]	77
2	amphetamines.mp. [mp=title, short title, abstract, full text, keywords, caption text]	46
3	amphetamine-like.mp. [mp=title, short title, abstract, full text, keywords, caption text]	77
4	1 or 2 or 3	93
5	limit 4 to (full systematic reviews and last 18 years)	75

	Search Group	Number of citations retrieved
1	cocaine.mp. [mp=title, short title, abstract, full text, keywords, caption text]	120
2	limit 1 to (full systematic reviews and last 18 years)	99

Peer-reviewed literature database searches for Level 1 studies

Amphetamine

Medline search results

#	Terms	Results
1	ATS.ti,ab.	3305
2	amphet*.ti,ab.	21976
3	meth?amphet*.ti,ab.	8943
4	deoxyephedrine.ti,ab.	3
5	desoxy*.ti,ab.	4962
6	madrine.ti,ab.	0
7	metamfet*.ti,ab.	11
8	methylamphet*.ti,ab.	388
9	n?methylamphet*.ti,ab.	1
10	d?amphet*.ti,ab.	11
11	dextro?amphet*.ti,ab.	599
12	dexamphet*.ti,ab.	333
13	dexedrine.ti,ab.	79
14	stimulant*.ti,ab.	21326
15	ecstasy.ti,ab.	3130
16	MDMA.ti,ab.	3391
17	lisdexamfetamine.ti,ab.	228
18	methylphenidate.ti,ab.	5661
19	modafinil.ti,ab.	1235
20	exp amphetamine/	18539
21	exp amphetamines/	35905
22	exp dextroamphetamine/	6889
23	exp p-chloroamphetamine/	643
24	exp 2,5-dimethoxy-4-methylamphetamine/	328
25	exp p-hydroxyamphetamine/	200
26	exp iofetamine/	884
27	exp methamphetamine/	8646

#	Terms	Results
28	exp benzphetamine/	324
29	exp phentermine/	1140
30	exp chlorphentermine/	307
31	exp mephentermine/	232
32	exp amphetamine-related disorders/	2694
33	exp n-methyl-3,4-methylenedioxyamphetamine/	3670
34	exp lisdexamfetamine dimesylate/	211
35	exp methylphenidate/	6603
36	1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10 or 11 or 12 or 13 or 14 or 15 or 16 or 17 or 18 or 19 or 20 or 21 or 22 or 23 or 24 or 25 or 26 or 27 or 28 or 29 or 30 or 31 or 32 or 33 or 34 or 35	76219
37	exp intravenous drug abuse/	13925
38	injecting risk.ti,ab.	129
39	"IDU$1".tw.	5019
40	"IVDU$1".tw.	718
41	"PWID$1".tw.	718
42	"injecting drug".tw.	3694
43	"intravenous drug".tw.	7165
44	"injecting substance".tw.	9
45	"intravenous substance".tw.	56
46	exp substance abuse, intravenous/	13925
47	37 or 38 or 39 or 40 or 41 or 42 or 43 or 44 or 45 or 46	21532
48	36 or 47	97100
49	exp intervention study/	790089
50	exp early intervention/	2495
51	drug dependence/di, dt, pc, rh, th [Diagnosis, Drug Therapy, Prevention, Rehabilitation, Therapy]	34941
52	exp substance abuse treatment centers/	5000
53	"drug dependence treatment".ti,ab.	100
54	exp harm reduction/	2347
55	Addiction/dt [Drug Therapy]	0
56	49 or 50 or 51 or 52 or 53 or 54 or 55	829093
57	(brief adj3 intervention).ti,ab.	3584
58	(safe adj3 inject*).ti,ab.	877
59	(needle adj2 syringe adj5 program).ti,ab.	66
60	exp condom/	9356
61	sexually transmitted disease/di, dt, pc, rh, th [Diagnosis, Drug Therapy, Prevention, Rehabilitation, Therapy]	12513
62	hepatitis C/di, dt, pc, rh, th [Diagnosis, Drug Therapy, Prevention, Rehabilitation, Therapy]	16277
63	Human immunodeficiency virus/pc [Prevention]	0
64	exp pre-exposure prophylaxis/	961
65	(prep adj5 HIV).ti,ab.	532
66	(prep adj5 sexual*).ti,ab.	72
67	(pre-exposure prophylaxis adj5 sexual*).mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]	109
68	(drug adj3 consum* adj3 (room or facil*)).ti,ab.	25
69	(supervis* adj3 inject*).ti,ab.	226
70	atypical antipsychotic agent/dt [Drug Therapy]	0
71	Suicide/pc [Prevention]	8402

#	Terms	Results
72	(suicide adj3 prevent*).ti,ab.	4249
73	exp behavior therapy/	65237
74	exp motivational interviewing/	1222
75	exp cognitive therapy/	23038
76	"cognitive behavio?r therapy".ti,ab.	2635
77	exp self-help groups/	9629
78	((peer or mutual) adj3 support*).ti,ab.	3835
79	exp family therapy/	8414
80	multisystemic therapy.ti,ab.	156
81	exp therapeutic community/	2116
82	agonist pharmacotherap*.ti,ab.	22
83	(drug adj3 (compulsory or detention)).ti,ab.	95
84	"NSP$1".tw.	4021
85	"needle syringe program$".tw.	47
86	"NSEP$1".tw.	56
87	"needle syringe exchange program$".tw.	23
88	"needle exchange$1".tw.	871
89	"syringe exchange$1".tw.	569
90	exp Needle-Exchange Programs/	1551
91	exp Harm Reduction/	2347
92	"HAART".tw.	10467
93	"Anti?Retroviral Treatment".tw.	6218
94	"Anti?Retroviral Therapy".tw.	31258
95	"highly active anti?retroviral therapy".tw.	9978
96	"highly active anti?retroviral treatment".tw.	491
97	"HIV treatment".tw.	3291
98	"anti-HIV Agents".tw.	757
99	"AIDS treatment".tw.	939
100	exp anti-hiv agents/	61737
101	exp hiv fusion inhibitors/	1136
102	exp hiv integrase inhibitors/	2139
103	exp hiv protease inhibitors/	12338
104	exp Antiretroviral Therapy, Highly Active/	19564
105	"contingency management".tw.	754
106	Vaccine/dt [Drug Therapy]	0
107	"detoxification".ti,ab.	23495
108	"drug detoxification".ti,ab.	296
109	exp social support/	62877
110	exp rehabilitation centers/	13595
111	exp "acceptance and commitment therapy"/	216
112	57 or 58 or 59 or 60 or 61 or 62 or 63 or 64 or 65 or 66 or 67 or 68 or 69 or 70 or 71 or 72 or 73 or 74 or 75 or 76 or 77 or 78 or 79 or 80 or 81 or 82 or 83 or 84 or 85 or 86 or 87 or 88 or 89 or 90 or 91 or 92 or 93 or 94 or 95 or 96 or 97 or 98 or 99 or 100 or 101 or 102 or 103 or 104 or 105 or 106 or 107 or 108 or 109 or 110 or 111	324497
113	56 or 112	1109346
114	exp Evaluation Studies/	233034
115	exp program evaluation/	67455
116	exp evidence based medicine/	67673

#	Terms	Results
117	exp "Outcome Assessment (Health Care)"/	921018
118	exp patient outcome assessment/	4985
119	exp randomized controlled trial/	455867
120	random* controlled trial.ti,ab.	61699
121	exp Clinical Trials as Topic/	311580
122	exp controlled clinical trial/	543249
123	multicenter study/	230085
124	random*.ti,ab.	825940
125	(pretest or pre test).ti,ab.	13379
126	(posttest or post test).ti,ab.	13989
127	before after.ti,ab.	3518
128	qua?irandomi*.ti,ab.	56
129	nonrandomi*.ti,ab.	9746
130	exp cohort analysis/	1720362
131	exp longitudinal study/	113428
132	exp Meta-Analysis as Topic/	16350
133	systematic review/	0
134	exp Clinical Trial/	790089
135	114 or 115 or 116 or 117 or 118 or 119 or 120 or 121 or 122 or 123 or 124 or 125 or 126 or 127 or 128 or 129 or 130 or 131 or 132 or 133 or 134	3593803
136	48 and 113 and 135	7913
137	limit 136 to (humans and yr="2000 -Current" and "review")	266

Searches conducted on 23/03/2018

Embase search results

#	Terms	Results
1	ATS.ti,ab.	7295
2	amphet*.ti,ab.	30659
3	meth?amphet*.ti,ab.	12636
4	deoxyephedrine.ti,ab.	9
5	desoxy*.ti,ab.	8941
6	madrine.ti,ab.	0
7	metamfet*.ti,ab.	16
8	methylamphet*.ti,ab.	650
9	n?methylamphet*.ti,ab.	4
10	d?amphet*.ti,ab.	62
11	dextro?amphet*.ti,ab.	882
12	dexamphet*.ti,ab.	799
13	dexedrine.ti,ab.	131
14	stimulant*.ti,ab.	32476
15	ecstasy.ti,ab.	4306
16	MDMA.ti,ab.	4632
17	lisdexamfetamine.ti,ab.	507
18	methylphenidate.ti,ab.	8903
19	modafinil.ti,ab.	2151
20	exp amphetamine/	35355
21	exp amphetamine derivative/	88963

#	Terms	Results
22	exp methamphetamine/	17689
23	exp dexamphetamine/	13922
24	exp iofetamine i 125/	41
25	exp iofetamine i 123/	1281
26	exp iofetamine/	216
27	exp 4 methoxyamphetamine/	283
28	exp hydroxyamphetamine/	653
29	exp mephentermine/	702
30	exp phentermine/	2665
31	exp benzphetamine/	1087
32	exp chloramphetamine/	1085
33	exp chlorphentermine/	735
34	exp midomafetamine/	467
35	exp methylphenidate/	20502
36	exp lisdexamfetamine/	1060
37	exp modafinil/	5092
38	1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10 or 11 or 12 or 13 or 14 or 15 or 16 or 17 or 18 or 19 or 20 or 21 or 22 or 23 or 24 or 25 or 26 or 27 or 28 or 29 or 30 or 31 or 32 or 33 or 34 or 35 or 36 or 37	154951
39	exp intravenous drug abuse/	9784
40	injecting risk.ti,ab.	175
41	"IDU$1".tw.	7487
42	"IVDU$1".tw.	1189
43	"PWID$1".tw.	1307
44	"injecting drug".tw.	4753
45	"intravenous drug".tw.	9605
46	"injecting substance".tw.	10
47	"intravenous substance".tw.	72
48	exp substance abuse, intravenous/	49527
49	39 or 40 or 41 or 42 or 43 or 44 or 45 or 46 or 47 or 48	72604
50	38 or 49	222036
51	exp intervention study/	35430
52	exp early intervention/	19363
53	drug dependence/di, dm, dt, pc, rh, th [Diagnosis, Disease Management, Drug Therapy, Prevention, Rehabilitation, Therapy]	7797
54	exp drug dependence treatment/	19705
55	exp residential care/	11221
56	exp harm reduction/	4534
57	Addiction/dt [Drug Therapy]	1413
58	51 or 52 or 53 or 54 or 55 or 56 or 57	95877
59	(brief adj3 intervention).ti,ab.	5654
60	(safe adj3 inject*).ti,ab.	1489
61	(needle adj2 syringe adj5 program).ti,ab.	109
62	exp condom/	18629
63	sexually transmitted disease/di, dm, dt, pc, rh, th [Diagnosis, Disease Management, Drug Therapy, Prevention, Rehabilitation, Therapy]	12456
64	hepatitis C/di, dm, dt, pc, rh, th [Diagnosis, Disease Management, Drug Therapy, Prevention, Rehabilitation, Therapy]	38575
65	Human immunodeficiency virus/dm, pc [Disease Management, Prevention]	7
66	exp pre-exposure prophylaxis/	1660

#	Terms	Results
67	(prep adj5 HIV).ti,ab.	996
68	(prep adj5 sexual*).ti,ab.	140
69	(pre-exposure prophylaxis adj5 sexual*).mp. [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword, floating subheading word]	76
70	(drug adj3 consum* adj3 (room or facil*)).ti,ab.	35
71	(supervis* adj3 inject*).ti,ab.	351
72	atypical antipsychotic agent/ct, dt [Clinical Trial, Drug Therapy]	7690
73	Suicide/pc	5910
74	(suicide adj3 prevent*).ti,ab.	5886
75	exp behavior therapy/	42863
76	exp motivational interviewing/	3338
77	exp cognitive behavioural therapy/	5043
78	exp self help/	12974
79	((peer or mutual) adj3 support*).ti,ab.	6276
80	exp family therapy/	12896
81	multisystemic therapy.ti,ab.	200
82	exp therapeutic community/	3051
83	agonist pharmacotherap*.ti,ab.	32
84	(drug adj3 (compulsory or detention)).ti,ab.	136
85	"NSP$1".tw.	5311
86	"needle syringe program$".tw.	75
87	"NSEP$1".tw.	81
88	"needle syringe exchange program$".tw.	33
89	"needle exchange$1".tw.	1078
90	"syringe exchange$1".tw.	725
91	exp preventive health service/	26240
92	"HAART".tw.	15971
93	"Anti?Retroviral Treatment".tw.	8878
94	"Anti?Retroviral Therapy".tw.	43929
95	"highly active anti?retroviral therapy".tw.	12656
96	"highly active anti?retroviral treatment".tw.	628
97	"HIV treatment".tw.	4851
98	"anti-HIV Agents".tw.	934
99	"AIDS treatment".tw.	1029
100	exp anti human immunodeficiency virus agent/	142530
101	exp human immunodeficiency virus fusion inhibitor/	12218
102	exp highly active antiretroviral therapy/	35463
103	"contingency management".tw.	1075
104	Vaccine/dt [Drug Therapy]	5049
105	detoxification/	23238
106	exp drug detoxification/	4363
107	exp psychosocial care/	15876
108	exp residential care/	11221
109	exp rehabilitation center/	13384
110	exp cognitive therapy/	43099
111	exp "acceptance and commitment therapy"/	851

#	Terms	Results
112	59 or 60 or 61 or 62 or 63 or 64 or 65 or 66 or 67 or 68 or 69 or 70 or 71 or 72 or 73 or 74 or 75 or 76 or 77 or 78 or 79 or 80 or 81 or 82 or 83 or 84 or 85 or 86 or 87 or 88 or 89 or 90 or 91 or 92 or 93 or 94 or 95 or 96 or 97 or 98 or 99 or 100 or 101 or 102 or 103 or 104 or 105 or 106 or 107 or 108 or 109 or 110 or 111	477954
113	58 or 112	551521
114	exp evaluation study/	46728
115	exp program evaluation/	15815
116	exp evidence based medicine/	956745
117	exp outcome assessment/	411185
118	exp randomized controlled trial/	491232
119	random* controlled trial.ti,ab.	96486
120	"clinical trial (topic)"/	91565
121	exp controlled clinical trial/	669443
122	multicenter study/	177890
123	random*.ti,ab.	1287665
124	(pretest or pre test).ti,ab.	21706
125	(posttest or post test).ti,ab.	22682
126	before after.ti,ab.	6543
127	qua?irandomi*.ti,ab.	115
128	nonrandomi*.ti,ab.	12767
129	exp open study/	30572
130	exp cohort analysis/	350020
131	exp longitudinal study/	110258
132	systematic review/	161232
133	"meta analysis (topic)"/	36687
134	114 or 115 or 116 or 117 or 118 or 119 or 120 or 121 or 122 or 123 or 124 or 125 or 126 or 127 or 128 or 129 or 130 or 131 or 132 or 133	2801496
135	50 and 113 and 134	6424
136	limit 135 to (human and yr="2000 -Current" and "review")	1315

Searches conducted on 21/03/2018

PsycINFO search results

#	Searches	Results
1	ATS.ti,ab.	449
2	Amphet*.ti,ab.	11725
3	meth?amphet*.ti,ab.	5024
4	deoxyephedrine.ti,ab.	0
5	desoxy*.ti,ab.	94
6	madrine.ti,ab.	0
7	metamfet*.ti,ab.	2
8	methylamphet*.ti,ab.	187
9	n?methylamphet*.ti,ab.	0
10	d?amphet*.ti,ab.	20
11	dextro?amphet*.ti,ab.	1571
12	dexamphet*.ti,ab.	185
13	dexedrine.ti,ab.	76
14	stimulant*.ti,ab.	10083
15	ecstasy.ti,ab.	2400

#	Searches	Results
16	MDMA.ti,ab.	1876
17	lisdexamfetamine.ti,ab.	179
18	methylphenidate.ti,ab.	4607
19	modafinil.ti,ab.	822
20	exp dexamphetamine/	2001
21	exp methamphetamine/	3660
22	exp amphetamine/	11072
23	exp methylenedioxymethamphetamine/	1962
24	exp methylphenidate/	3473
25	exp dextroamphetamine/	2001
26	1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10 or 11 or 12 or 13 or 14 or 15 or 16 or 17 or 18 or 19 or 20 or 21 or 22 or 23 or 24 or 25	31236
27	exp Intravenous Drug Usage/	3667
28	injecting risk.ti,ab.	107
29	"IDU$1".tw.	2123
30	"IVDU$1".tw.	119
31	"PWID$1".tw.	582
32	"injecting drug".tw.	1789
33	"intravenous drug".tw.	1022
34	"intravenous substance".tw.	13
35	"injecting substance".tw.	5
36	27 or 28 or 29 or 30 or 31 or 32 or 33 or 34 or 35	5748
37	26 or 36	36634
38	exp intervention/	90946
39	exp early intervention/	9952
40	exp drug dependency/	24734
41	exp drug therapy/	134504
42	"drug dependence treatment".ti,ab.	87
43	exp harm reduction/	3128
44	exp Addiction/	56150
45	38 or 39 or 40 or 41 or 42 or 43 or 44	285091
46	(brief adj3 intervention).ti,ab.	3978
47	(safe adj3 inject*).ti,ab.	103
48	(needle adj2 syringe adj5 program).ti,ab.	66
49	exp condom/	3696
50	exp sexually transmitted disease/	42680
51	("Hepatitis C" or "HCV").ti,ab.	2734
52	exp HIV/	39638
53	(prep adj5 HIV).ti,ab.	220
54	(prep adj5 sexual*).ti,ab.	41
55	(pre-exposure prophylaxis adj5 sexual*).mp. [mp=title, abstract, heading word, table of contents, key concepts, original title, tests & measures]	8
56	(drug adj3 consum* adj3 (room or facil*)).ti,ab.	22
57	(supervis* adj3 inject*).ti,ab.	167
58	"atypical antipsychotic agent".ti,ab.	166
59	exp Suicide/	25646
60	(suicide adj3 prevent*).ti,ab.	5596
61	exp behavior therapy/	18948

#	Searches	Results
62	exp motivational interviewing/	2127
63	exp cognitive behavior therapy/	18012
64	exp self-help techniques/	9853
65	exp support groups/	5707
66	((peer or mutual) adj3 support*).ti,ab.	5906
67	exp family therapy/	21144
68	multisystemic therapy.ti,ab.	408
69	exp therapeutic community/	2740
70	agonist pharmacotherap*.ti,ab.	20
71	(drug adj3 (compulsory or detention)).ti,ab.	80
72	"NSP$1".tw.	359
73	"needle syringe program$".tw.	68
74	"NSEP$1".tw.	17
75	"needle syringe exchange program$".tw.	25
76	"needle exchange$1".tw.	509
77	"syringe exchange$1".tw.	404
78	exp preventive medicine/	2017
79	"HAART".tw.	1249
80	"Anti?Retroviral Treatment".tw.	953
81	"Anti?Retroviral Treatment".tw.	953
82	"Anti?Retroviral Therapy".tw.	4140
83	"highly active anti?retroviral therapy".tw.	1084
84	"highly active anti?retroviral treatment".tw.	68
85	"HIV treatment".tw.	1067
86	"anti-HIV Agents".tw.	5
87	"AIDS treatment".tw.	248
88	"anti human immunodeficiency virus agent".ti,ab.	0
89	"human immunodeficiency virus fusion inhibitor".ti,ab.	0
90	"contingency management".tw.	1602
91	exp Immunization/	4074
92	detoxification/	1682
93	exp drug rehabilitation/	28656
94	exp psychosocial rehabilitation/	10806
95	exp rehabilitation centers/	1026
96	exp cognitive therapy/	12906
97	exp "acceptance and commitment therapy"/	1425
98	46 or 47 or 48 or 49 or 50 or 51 or 52 or 53 or 54 or 55 or 56 or 57 or 58 or 59 or 60 or 61 or 62 or 63 or 64 or 65 or 66 or 67 or 68 or 69 or 70 or 71 or 72 or 73 or 74 or 75 or 76 or 77 or 78 or 79 or 80 or 81 or 82 or 83 or 84 or 85 or 86 or 87 or 88 or 89 or 90 or 91 or 92 or 93 or 94 or 95 or 96 or 97	209056
99	26 or 98	238254
100	exp treatment effectiveness evaluation/	22334
101	exp program evaluation/	19262
102	exp evidence based practice/	15860
103	"outcome assessment".ti,ab.	870
104	random* controlled trial.ti,ab.	16760
105	exp clinical trials/	10832
106	"controlled clinical trial".ti,ab.	1309
107	"multicenter study".ti,ab.	1361

#	Searches	Results
108	random*.ti,ab.	175649
109	(pretest or pre test).ti,ab.	16342
110	(posttest or post test).ti,ab.	21983
111	before after.ti,ab.	820
112	qua?irandomi*.ti,ab.	12
113	nonrandomi*.ti,ab.	879
114	exp cohort analysis/	1248
115	exp longitudinal studies/	15911
116	"systematic review".ti,ab.	19694
117	exp meta analysis/	4149
118	100 or 101 or 102 or 103 or 104 or 105 or 106 or 107 or 108 or 109 or 110 or 111 or 112 or 113 or 114 or 115 or 116 or 117	281692
119	37 and 99 and 118	1971
120	limit 119 to (human and "reviews (best balance of sensitivity and specificity)" and yr="2000 -Current")	1235

Searches conducted on 23/03/2018

Cocaine

Medline search results

#	Terms	Results
1	cocaine*.ti,ab.	32131
2	exp cocaine/	24119
3	exp Crack Cocaine/	1327
4	exp cocaine-related disorders/	7472
5	exp cocaine smoking/	2
6	1 or 2 or 3 or 4 or 5	37286
7	exp intravenous drug abuse/	13925
8	injecting risk.ti,ab.	129
9	"IDU$1".tw.	5019
10	"IVDU$1".tw.	718
11	"PWID$1".tw.	718
12	"injecting drug".tw.	3694
13	"intravenous drug".tw.	7165
14	"injecting substance".tw.	9
15	"intravenous substance".tw.	56
16	exp substance abuse, intravenous/	13925
17	7 or 8 or 9 or 10 or 11 or 12 or 13 or 14 or 15 or 16	21532
18	6 or 17	57503
19	exp intervention study/	790089
20	exp early intervention/	2495
21	drug dependence/di, dt, pc, rh, th [Diagnosis, Drug Therapy, Prevention, Rehabilitation, Therapy]	34941
22	exp substance abuse treatment centers/	5000
23	"drug dependence treatment".ti,ab.	100
24	exp harm reduction/	2347
25	Addiction/dt [Drug Therapy]	0
26	19 or 20 or 21 or 22 or 23 or 24 or 25	829093
27	(brief adj3 intervention).ti,ab.	3584
28	(safe adj3 inject*).ti,ab.	877
29	(needle adj2 syringe adj5 program).ti,ab.	66

#	Terms	Results
30	exp condom/	9356
31	sexually transmitted disease/di, dt, pc, rh, th [Diagnosis, Drug Therapy, Prevention, Rehabilitation, Therapy]	12513
32	hepatitis C/di, dt, pc, rh, th [Diagnosis, Drug Therapy, Prevention, Rehabilitation, Therapy]	16277
33	Human immunodeficiency virus/pc [Prevention]	0
34	exp pre-exposure prophylaxis/	961
35	(prep adj5 HIV).ti,ab.	532
36	(prep adj5 sexual*).ti,ab.	72
37	(pre-exposure prophylaxis adj5 sexual*).mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]	109
38	(drug adj3 consum* adj3 (room or facil*)).ti,ab.	25
39	(supervis* adj3 inject*).ti,ab.	226
40	atypical antipsychotic agent/dt [Drug Therapy]	0
41	Suicide/pc [Prevention]	8402
42	(suicide adj3 prevent*).ti,ab.	4249
43	exp behavior therapy/	65237
44	exp motivational interviewing/	1222
45	exp cognitive therapy/	23038
46	"cognitive behavio?r therapy".ti,ab.	2635
47	exp self-help groups/	9629
48	((peer or mutual) adj3 support*).ti,ab.	3835
49	exp family therapy/	8414
50	multisystemic therapy.ti,ab.	156
51	exp therapeutic community/	2116
52	agonist pharmacotherap*.ti,ab.	22
53	(drug adj3 (compulsory or detention)).ti,ab.	95
54	"NSP$1".tw.	4021
55	"needle syringe program$".tw.	47
56	"NSEP$1".tw.	56
57	"needle syringe exchange program$".tw.	23
58	"needle exchange$1".tw.	871
59	"syringe exchange$1".tw.	569
60	exp Needle-Exchange Programs/	1551
61	exp Harm Reduction/	2347
62	"HAART".tw.	10467
63	"Anti?Retroviral Treatment".tw.	6218
64	"Anti?Retroviral Therapy".tw.	31258
65	"highly active anti?retroviral therapy".tw.	9978
66	"highly active anti?retroviral treatment".tw.	491
67	"HIV treatment".tw.	3291
68	"anti-HIV Agents".tw.	757
69	"AIDS treatment".tw.	939
70	exp anti-hiv agents/	61737
71	exp hiv fusion inhibitors/	1136
72	exp hiv integrase inhibitors/	2139
73	exp hiv protease inhibitors/	12338
74	exp Antiretroviral Therapy, Highly Active/	19564

#	Terms	Results
75	"contingency management".tw.	754
76	Vaccine/dt [Drug Therapy]	0
77	"detoxification".ti,ab.	23495
78	"drug detoxification".ti,ab.	296
79	exp social support/	62877
80	exp rehabilitation centers/	13595
81	exp "acceptance and commitment therapy"/	216
82	27 or 28 or 29 or 30 or 31 or 32 or 33 or 34 or 35 or 36 or 37 or 38 or 39 or 40 or 41 or 42 or 43 or 44 or 45 or 46 or 47 or 48 or 49 or 50 or 51 or 52 or 53 or 54 or 55 or 56 or 57 or 58 or 59 or 60 or 61 or 62 or 63 or 64 or 65 or 66 or 67 or 68 or 69 or 70 or 71 or 72 or 73 or 74 or 75 or 76 or 77 or 78 or 79 or 80 or 81	324497
83	26 or 82	1109346
84	exp Evaluation Studies/	233034
85	exp program evaluation/	67455
86	exp evidence based medicine/	67673
87	exp "Outcome Assessment (Health Care)"/	921018
88	exp patient outcome assessment/	4985
89	exp randomized controlled trial/	455867
90	random* controlled trial.ti,ab.	61699
91	exp Clinical Trials as Topic/	311580
92	exp controlled clinical trial/	543249
93	multicenter study/	230085
94	random*.ti,ab.	825940
95	(pretest or pre test).ti,ab.	13379
96	(posttest or post test).ti,ab.	13989
97	before after.ti,ab.	3518
98	qua?irandomi*.ti,ab.	56
99	nonrandomi*.ti,ab.	9746
100	exp cohort analysis/	1720362
101	exp longitudinal study/	113428
102	exp Meta-Analysis as Topic/	16350
103	systematic review/	0
104	exp Clinical Trial/	790089
105	84 or 85 or 86 or 87 or 88 or 89 or 90 or 91 or 92 or 93 or 94 or 95 or 96 or 97 or 98 or 99 or 100 or 101 or 102 or 103 or 104	3593803
106	18 and 83 and 105	5461
107	limit 106 to (humans and yr="2000 -Current" and "review")	219

Searches conducted on 23/03/2018

Embase search results

#	Terms	Results
1	cocaine*.ti,ab.	44389
2	exp cocaine/	53566
3	exp cocaine dependence/	11571
4	exp cocaine derivative/	595
5	1 or 2 or 3 or 4	63942
6	exp intravenous drug abuse/	9784
7	injecting risk.ti,ab.	175
8	"IDU$1".tw.	7487
9	"IVDU$1".tw.	1189

#	Terms	Results
10	"PWID$1".tw.	1307
11	"injecting drug".tw.	4753
12	"intravenous drug".tw.	9605
13	"injecting substance".tw.	10
14	"intravenous substance".tw.	72
15	exp substance abuse, intravenous/	49527
16	6 or 7 or 8 or 9 or 10 or 11 or 12 or 13 or 14 or 15	72604
17	5 or 16	129176
18	exp intervention study/	35430
19	exp early intervention/	19363
20	drug dependence/di, dm, dt, pc, rh, th [Diagnosis, Disease Management, Drug Therapy, Prevention, Rehabilitation, Therapy]	7797
21	exp drug dependence treatment/	19705
22	exp residential care/	11221
23	exp harm reduction/	4534
24	Addiction/dt [Drug Therapy]	1413
25	18 or 19 or 20 or 21 or 22 or 23 or 24	95877
26	(brief adj3 intervention).ti,ab.	5654
27	(safe adj3 inject*).ti,ab.	1489
28	(needle adj2 syringe adj5 program).ti,ab.	109
29	exp condom/	18629
30	sexually transmitted disease/di, dm, dt, pc, rh, th [Diagnosis, Disease Management, Drug Therapy, Prevention, Rehabilitation, Therapy]	12456
31	hepatitis C/di, dm, dt, pc, rh, th [Diagnosis, Disease Management, Drug Therapy, Prevention, Rehabilitation, Therapy]	38575
32	Human immunodeficiency virus/dm, pc [Disease Management, Prevention]	7
33	exp pre-exposure prophylaxis/	1660
34	(prep adj5 HIV).ti,ab.	996
35	(prep adj5 sexual*).ti,ab.	140
36	(pre-exposure prophylaxis adj5 sexual*).mp. [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword, floating subheading word]	76
37	(drug adj3 consum* adj3 (room or facil*)).ti,ab.	35
38	(supervis* adj3 inject*).ti,ab.	351
39	atypical antipsychotic agent/ct, dt [Clinical Trial, Drug Therapy]	7690
40	Suicide/pc	5910
41	(suicide adj3 prevent*).ti,ab.	5886
42	exp behavior therapy/	42863
43	exp motivational interviewing/	3338
44	exp cognitive behavioural therapy/	5043
45	exp self help/	12974
46	((peer or mutual) adj3 support*).ti,ab.	6276
47	exp family therapy/	12896
48	multisystemic therapy.ti,ab.	200
49	exp therapeutic community/	3051
50	agonist pharmacotherap*.ti,ab.	32
51	(drug adj3 (compulsory or detention)).ti,ab.	136
52	"NSP$1".tw.	5311
53	"needle syringe program$".tw.	75
54	"NSEP$1".tw.	81
55	"needle syringe exchange program$".tw.	33
56	"needle exchange$1".tw.	1078
57	"syringe exchange$1".tw.	725
58	exp preventive health service/	26240
59	"HAART".tw.	15971
60	"Anti?Retroviral Treatment".tw.	8878
61	"Anti?Retroviral Therapy".tw.	43929
62	"highly active anti?retroviral therapy".tw.	12656

#	Terms	Results
63	"highly active anti?retroviral treatment".tw.	628
64	"HIV treatment".tw.	4851
65	"anti-HIV Agents".tw.	934
66	"AIDS treatment".tw.	1029
67	exp anti human immunodeficiency virus agent/	142530
68	exp human immunodeficiency virus fusion inhibitor/	12218
69	exp highly active antiretroviral therapy/	35463
70	"contingency management".tw.	1075
71	Vaccine/dt [Drug Therapy]	5049
72	detoxification/	23238
73	exp drug detoxification/	4363
74	exp psychosocial care/	15876
75	exp residential care/	11221
76	exp rehabilitation center/	13384
77	exp cognitive therapy/	43099
78	exp "acceptance and commitment therapy"/	851
79	26 or 27 or 28 or 29 or 30 or 31 or 32 or 33 or 34 or 35 or 36 or 37 or 38 or 39 or 40 or 41 or 42 or 43 or 44 or 45 or 46 or 47 or 48 or 49 or 50 or 51 or 52 or 53 or 54 or 55 or 56 or 57 or 58 or 59 or 60 or 61 or 62 or 63 or 64 or 65 or 66 or 67 or 68 or 69 or 70 or 71 or 72 or 73 or 74 or 75 or 76 or 77 or 78	477954
80	25 or 79	551521
81	exp evaluation study/	46728
82	exp program evaluation/	15815
83	exp evidence based medicine/	956745
84	exp outcome assessment/	411185
85	exp randomized controlled trial/	491232
86	random* controlled trial.ti,ab.	96486
87	"clinical trial (topic)"/	91565
88	exp controlled clinical trial/	669443
89	multicenter study/	177890
90	random*.ti,ab.	1287665
91	(pretest or pre test).ti,ab.	21706
92	(posttest or post test).ti,ab.	22682
93	before after.ti,ab.	6543
94	qua?irandomi*.ti,ab.	115
95	nonrandomi*.ti,ab.	12767
96	exp open study/	30572
97	exp cohort analysis/	350020
98	exp longitudinal study/	110258
99	systematic review/	161232
100	"meta analysis (topic)"/	36687
101	81 or 82 or 83 or 84 or 85 or 86 or 87 or 88 or 89 or 90 or 91 or 92 or 93 or 94 or 95 or 96 or 97 or 98 or 99 or 100	2801496
102	17 and 80 and 101	5952
103	limit 102 to (human and yr="2000 -Current" and "review")	822

Searches conducted on 21/03/2018

PsycINFO search results

#	Terms	Results
1	cocaine*.ti,ab.	19589
2	exp Crack Cocaine/	600
3	exp cocaine/	13205
4	1 or 2 or 3	19964
5	exp Intravenous Drug Usage/	3667
6	injecting risk.ti,ab.	107
7	"IDU$1".tw.	2123

#	Terms	Results
8	"IVDU$1".tw.	119
9	"PWID$1".tw.	582
10	"injecting drug".tw.	1789
11	"intravenous drug".tw.	1022
12	"intravenous substance".tw.	13
13	"injecting substance".tw.	5
14	5 or 6 or 7 or 8 or 9 or 10 or 11 or 12 or 13	5748
15	4 or 14	25124
16	exp intervention/	90946
17	exp early intervention/	9952
18	exp drug dependency/	24734
19	exp drug therapy/	134504
20	"drug dependence treatment".ti,ab.	87
21	exp harm reduction/	3128
22	exp Addiction/	56150
23	16 or 17 or 18 or 19 or 20 or 21 or 22	285091
24	(brief adj3 intervention).ti,ab.	3978
25	(safe adj3 inject*).ti,ab.	103
26	(needle adj2 syringe adj5 program).ti,ab.	66
27	exp condom/	3696
28	exp sexually transmitted disease/	42680
29	("Hepatitis C" or "HCV").ti,ab.	2734
30	exp HIV/	39638
31	(prep adj5 HIV).ti,ab.	220
32	(prep adj5 sexual*).ti,ab.	41
33	(pre-exposure prophylaxis adj5 sexual*).mp. [mp=title, abstract, heading word, table of contents, key concepts, original title, tests & measures]	8
34	(drug adj3 consum* adj3 (room or facil*)).ti,ab.	22
35	(supervis* adj3 inject*).ti,ab.	167
36	"atypical antipsychotic agent".ti,ab.	166
37	exp Suicide/	25646
38	(suicide adj3 prevent*).ti,ab.	5596
39	exp behavior therapy/	18948
40	exp motivational interviewing/	2127
41	exp cognitive behavior therapy/	18012
42	exp self-help techniques/	9853
43	exp support groups/	5707
44	((peer or mutual) adj3 support*).ti,ab.	5906
45	exp family therapy/	21144
46	multisystemic therapy.ti,ab.	408
47	exp therapeutic community/	2740
48	agonist pharmacotherap*.ti,ab.	20
49	(drug adj3 (compulsory or detention)).ti,ab.	80
50	"NSP$1".tw.	359
51	"needle syringe program$".tw.	68
52	"NSEP$1".tw.	17
53	"needle syringe exchange program$".tw.	25
54	"needle exchange$1".tw.	509
55	"syringe exchange$1".tw.	404
56	exp preventive medicine/	2017
57	"HAART".tw.	1249
58	"Anti?Retroviral Treatment".tw.	953

#	Terms	Results
59	"Anti?Retroviral Treatment".tw.	953
60	"Anti?Retroviral Therapy".tw.	4140
61	"highly active anti?retroviral therapy".tw.	1084
62	"highly active anti?retroviral treatment".tw.	68
63	"HIV treatment".tw.	1067
64	"anti-HIV Agents".tw.	5
65	"AIDS treatment".tw.	248
66	"anti human immunodeficiency virus agent".ti,ab.	0
67	"human immunodeficiency virus fusion inhibitor".ti,ab.	0
68	"contingency management".tw.	1602
69	exp Immunization/	4074
70	detoxification/	1682
71	exp drug rehabilitation/	28656
72	exp psychosocial rehabilitation/	10806
73	exp rehabilitation centers/	1026
74	exp cognitive therapy/	12906
75	exp "acceptance and commitment therapy"/	1425
76	24 or 25 or 26 or 27 or 28 or 29 or 30 or 31 or 32 or 33 or 34 or 35 or 36 or 37 or 38 or 39 or 40 or 41 or 42 or 43 or 44 or 45 or 46 or 47 or 48 or 49 or 50 or 51 or 52 or 53 or 54 or 55 or 56 or 57 or 58 or 59 or 60 or 61 or 62 or 63 or 64 or 65 or 66 or 67 or 68 or 69 or 70 or 71 or 72 or 73 or 74 or 75	209056
77	23 or 76	450255
78	exp treatment effectiveness evaluation/	22334
79	exp program evaluation/	19262
80	exp evidence based practice/	15860
81	"outcome assessment".ti,ab.	870
82	random* controlled trial.ti,ab.	16760
83	exp clinical trials/	10832
84	"controlled clinical trial".ti,ab.	1309
85	"multicenter study".ti,ab.	1361
86	random*.ti,ab.	175649
87	(pretest or pre test).ti,ab.	16342
88	(posttest or post test).ti,ab.	21983
89	before after.ti,ab.	820
90	qua?irandomi*.ti,ab.	12
91	nonrandomi*.ti,ab.	879
92	exp cohort analysis/	1248
93	exp longitudinal studies/	15911
94	"systematic review".ti,ab.	19694
95	exp meta analysis/	4149
96	78 or 79 or 80 or 81 or 82 or 83 or 84 or 85 or 86 or 87 or 88 or 89 or 90 or 91 or 92 or 93 or 94 or 95	281692
97	15 and 77 and 96	1489
98	limit 97 to (human and "reviews (best balance of sensitivity and specificity)" and yr="2000 - Current")	825

Searches conducted on 22/03/2018

Peer-reviewed literature database searches for Level 2-4 studies

Embase

Medline search results

#	Terms	Results
1	ATS.ti,ab.	7495
2	amphet*.ti,ab.	31111
3	meth?amphet*.ti,ab.	13155
4	deoxyephedrine.ti,ab.	9
5	desoxy*.ti,ab.	8962
6	madrine.ti,ab.	0
7	metamfet*.ti,ab.	16
8	methylamphet*.ti,ab.	657
9	n?methylamphet*.ti,ab.	4
10	d?amphet*.ti,ab.	62
11	dextro?amphet*.ti,ab.	890
12	dexamphet*.ti,ab.	806
13	dexedrine.ti,ab.	131
14	stimulant*.ti,ab.	32998
15	ecstasy.ti,ab.	4384
16	MDMA.ti,ab.	4739
17	lisdexamfetamine.ti,ab.	524
18	methylphenidate.ti,ab.	9064
19	modafinil.ti,ab.	2195
20	exp amphetamine/	35736
21	exp amphetamine derivative/	90357
22	exp methamphetamine/	18273
23	exp dexamphetamine/	14027
24	exp iofetamine i 125/	41
25	exp iofetamine i 123/	1296
26	exp iofetamine/	217
27	exp 4 methoxyamphetamine/	288
28	exp hydroxyamphetamine/	659
29	exp mephentermine/	705
30	exp phentermine/	2705
31	exp benzphetamine/	1091
32	exp chloramphetamine/	1094
33	exp chlorphentermine/	737
34	exp midomafetamine/	592
35	exp methylphenidate/	20814
36	exp lisdexamfetamine/	1103
37	exp modafinil/	5200
38	1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10 or 11 or 12 or 13 or 14 or 15 or 16 or 17 or 18 or 19 or 20 or 21 or 22 or 23 or 24 or 25 or 26 or 27 or 28 or 29 or 30 or 31 or 32 or 33 or 34 or 35 or 36 or 37	157370
39	exp intravenous drug abuse/	9955
40	injecting risk.ti,ab.	180
41	"IDU$1".tw.	7574
42	"IVDU$1".tw.	1218
43	"PWID$1".tw.	1483
44	"injecting drug".tw.	4835
45	"intravenous drug".tw.	9754
46	"injecting substance".tw.	10

#	Terms	Results
47	"intravenous substance".tw.	73
48	exp substance abuse, intravenous/	50328
49	39 or 40 or 41 or 42 or 43 or 44 or 45 or 46 or 47 or 48	73900
50	38 or 49	225651
51	exp intervention study/	36867
52	exp early intervention/	20213
53	drug dependence/di, dm, dt, pc, rh, th [Diagnosis, Disease Management, Drug Therapy, Prevention, Rehabilitation, Therapy]	8099
54	exp drug dependence treatment/	20146
55	exp residential care/	11410
56	exp harm reduction/	4747
57	Addiction/dt [Drug Therapy]	1421
58	51 or 52 or 53 or 54 or 55 or 56 or 57	99220
59	(brief adj3 intervention).ti,ab.	5857
60	(safe adj3 inject*).ti,ab.	1547
61	(needle adj2 syringe adj5 program).ti,ab.	115
62	exp condom/	18849
63	sexually transmitted disease/di, dm, dt, pc, rh, th [Diagnosis, Disease Management, Drug Therapy, Prevention, Rehabilitation, Therapy]	12598
64	hepatitis C/di, dm, dt, pc, rh, th [Diagnosis, Disease Management, Drug Therapy, Prevention, Rehabilitation, Therapy]	39198
65	Human immunodeficiency virus/dm, pc [Disease Management, Prevention]	7
66	exp pre-exposure prophylaxis/	1915
67	(prep adj5 HIV).ti,ab.	1153
68	(prep adj5 sexual*).ti,ab.	165
69	(pre-exposure prophylaxis adj5 sexual*).mp. [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword, floating subheading word, candidate term word]	81
70	(drug adj3 consum* adj3 (room or facil*)).ti,ab.	37
71	(supervis* adj3 inject*).ti,ab.	359
72	atypical antipsychotic agent/ct, dt [Clinical Trial, Drug Therapy]	7814
73	Suicide/pc	6027
74	(suicide adj3 prevent*).ti,ab.	6092
75	exp behavior therapy/	43407
76	exp motivational interviewing/	3579
77	exp cognitive behavioural therapy/	6008
78	exp self help/	13126
79	((peer or mutual) adj3 support*).ti,ab.	6600
80	exp family therapy/	13070
81	multisystemic therapy.ti,ab.	202
82	exp therapeutic community/	3070
83	agonist pharmacotherap*.ti,ab.	37
84	(drug adj3 (compulsory or detention)).ti,ab.	138
85	"NSP$1".tw.	5445
86	"needle syringe program$".tw.	78
87	"NSEP$1".tw.	85
88	"needle syringe exchange program$".tw.	35
89	"needle exchange$1".tw.	1095

#	Terms	Results
90	"syringe exchange$1".tw.	748
91	exp preventive health service/	26651
92	"HAART".tw.	16179
93	"Anti?Retroviral Treatment".tw.	9110
94	"Anti?Retroviral Therapy".tw.	45363
95	"highly active anti?retroviral therapy".tw.	12798
96	"highly active anti?retroviral treatment".tw.	634
97	"HIV treatment".tw.	5046
98	"anti-HIV Agents".tw.	943
99	"AIDS treatment".tw.	1046
100	exp anti human immunodeficiency virus agent/	145547
101	exp human immunodeficiency virus fusion inhibitor/	12567
102	exp highly active antiretroviral therapy/	35852
103	"contingency management".tw.	1106
104	Vaccine/dt [Drug Therapy]	5145
105	detoxification/	23671
106	exp drug detoxification/	4429
107	exp psychosocial care/	16375
108	exp residential care/	11410
109	exp rehabilitation center/	13630
110	exp cognitive therapy/	43684
111	exp "acceptance and commitment therapy"/	920
112	59 or 60 or 61 or 62 or 63 or 64 or 65 or 66 or 67 or 68 or 69 or 70 or 71 or 72 or 73 or 74 or 75 or 76 or 77 or 78 or 79 or 80 or 81 or 82 or 83 or 84 or 85 or 86 or 87 or 88 or 89 or 90 or 91 or 92 or 93 or 94 or 95 or 96 or 97 or 98 or 99 or 100 or 101 or 102 or 103 or 104 or 105 or 106 or 107 or 108 or 109 or 110 or 111	488458
113	58 or 112	564827
114	exp evaluation study/	49690
115	exp program evaluation/	17083
116	exp evidence based medicine/	995049
117	exp outcome assessment/	434786
118	exp randomized controlled trial/	507672
119	random* controlled trial.ti,ab.	100454
120	"clinical trial (topic)"/	94079
121	exp controlled clinical trial/	690327
122	multicenter study/	188788
123	random*.ti,ab.	1324555
124	(pretest or pre test).ti,ab.	22537
125	(posttest or post test).ti,ab.	23627
126	before after.ti,ab.	6772
127	qua?irandomi*.ti,ab.	115
128	nonrandomi*.ti,ab.	13067
129	exp open study/	32024
130	exp cohort analysis/	383288
131	exp longitudinal study/	115056
132	systematic review/	171907
133	"meta analysis (topic)"/	38039

#	Terms	Results
134	114 or 115 or 116 or 117 or 118 or 119 or 120 or 121 or 122 or 123 or 124 or 125 or 126 or 127 or 128 or 129 or 130 or 131 or 132 or 133	2917168
135	"OST".tw.	2019
136	"opioid substitution".tw.	843
137	"methadone".tw.	17228
138	"MMT".tw.	3668
139	"methadone maintenance".tw.	4850
140	"buprenorphine".tw.	7895
141	"Buprenorphine maintenance".tw.	343
142	"opioid replacement".tw.	160
143	"opioid agonist".tw.	3335
144	"opiate agonist".tw.	607
145	"opioid maintenance".tw.	528
146	"opiate maintenance".tw.	148
147	exp Buprenorphine/	15094
148	exp Methadone/	30629
149	exp Opiate Substitution Treatment/	1720
150	exp methadone treatment/	4247
151	exp buprenorphine plus naloxone/	1368
152	135 or 136 or 137 or 138 or 139 or 140 or 141 or 142 or 143 or 144 or 145 or 146 or 147 or 148 or 149 or 150 or 151	51124
153	113 or 152	602761
154	50 and 134 and 153	7166
155	limit 154 to (human and yr="2000 -Current")	6510

Search conducted on 02/07/2018

Cocaine

#	Terms	Results
1	cocaine*.ti,ab.	45307
2	exp cocaine/	54566
3	exp cocaine dependence/	11836
4	exp cocaine derivative/	599
5	1 or 2 or 3 or 4	65167
6	exp intravenous drug abuse/	9955
7	injecting risk.ti,ab.	180
8	"IDU$1".tw.	7574
9	"IVDU$1".tw.	1218
10	"PWID$1".tw.	1483
11	"injecting drug".tw.	4835
12	"intravenous drug".tw.	9754
13	"injecting substance".tw.	10
14	"intravenous substance".tw.	73
15	exp substance abuse, intravenous/	50328
16	6 or 7 or 8 or 9 or 10 or 11 or 12 or 13 or 14 or 15	73900
17	5 or 16	131612
18	exp intervention study/	36867
19	exp early intervention/	20213
20	drug dependence/di, dm, dt, pc, rh, th [Diagnosis, Disease Management, Drug Therapy, Prevention, Rehabilitation, Therapy]	8099

#	Terms	Results
21	exp drug dependence treatment/	20146
22	exp residential care/	11410
23	exp harm reduction/	4747
24	Addiction/dt [Drug Therapy]	1421
25	18 or 19 or 20 or 21 or 22 or 23 or 24	99220
26	(brief adj3 intervention).ti,ab.	5857
27	(safe adj3 inject*).ti,ab.	1547
28	(needle adj2 syringe adj5 program).ti,ab.	115
29	exp condom/	18849
30	sexually transmitted disease/di, dm, dt, pc, rh, th [Diagnosis, Disease Management, Drug Therapy, Prevention, Rehabilitation, Therapy]	12598
31	hepatitis C/di, dm, dt, pc, rh, th [Diagnosis, Disease Management, Drug Therapy, Prevention, Rehabilitation, Therapy]	39198
32	Human immunodeficiency virus/dm, pc [Disease Management, Prevention]	7
33	exp pre-exposure prophylaxis/	1915
34	(prep adj5 HIV).ti,ab.	1153
35	(prep adj5 sexual*).ti,ab.	165
36	(pre-exposure prophylaxis adj5 sexual*).mp. [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword, floating subheading word, candidate term word]	81
37	(drug adj3 consum* adj3 (room or facil*)).ti,ab.	37
38	(supervis* adj3 inject*).ti,ab.	359
39	atypical antipsychotic agent/ct, dt [Clinical Trial, Drug Therapy]	7814
40	Suicide/pc	6027
41	(suicide adj3 prevent*).ti,ab.	6092
42	exp behavior therapy/	43407
43	exp motivational interviewing/	3579
44	exp cognitive behavioural therapy/	6008
45	exp self help/	13126
46	((peer or mutual) adj3 support*).ti,ab.	6600
47	exp family therapy/	13070
48	multisystemic therapy.ti,ab.	202
49	exp therapeutic community/	3070
50	agonist pharmacotherap*.ti,ab.	37
51	(drug adj3 (compulsory or detention)).ti,ab.	138
52	"NSP$1".tw.	5445
53	"needle syringe program$".tw.	78
54	"NSEP$1".tw.	85
55	"needle syringe exchange program$".tw.	35
56	"needle exchange$1".tw.	1095
57	"syringe exchange$1".tw.	748
58	exp preventive health service/	26651
59	"HAART".tw.	16179
60	"Anti?Retroviral Treatment".tw.	9110
61	"Anti?Retroviral Therapy".tw.	45363
62	"highly active anti?retroviral therapy".tw.	12798
63	"highly active anti?retroviral treatment".tw.	634

#	Terms	Results
64	"HIV treatment".tw.	5046
65	"anti-HIV Agents".tw.	943
66	"AIDS treatment".tw.	1046
67	exp anti human immunodeficiency virus agent/	145547
68	exp human immunodeficiency virus fusion inhibitor/	12567
69	exp highly active antiretroviral therapy/	35852
70	"contingency management".tw.	1106
71	Vaccine/dt [Drug Therapy]	5145
72	detoxification/	23671
73	exp drug detoxification/	4429
74	exp psychosocial care/	16375
75	exp residential care/	11410
76	exp rehabilitation center/	13630
77	exp cognitive therapy/	43684
78	exp "acceptance and commitment therapy"/	920
79	26 or 27 or 28 or 29 or 30 or 31 or 32 or 33 or 34 or 35 or 36 or 37 or 38 or 39 or 40 or 41 or 42 or 43 or 44 or 45 or 46 or 47 or 48 or 49 or 50 or 51 or 52 or 53 or 54 or 55 or 56 or 57 or 58 or 59 or 60 or 61 or 62 or 63 or 64 or 65 or 66 or 67 or 68 or 69 or 70 or 71 or 72 or 73 or 74 or 75 or 76 or 77 or 78	488458
80	25 or 79	564827
81	exp evaluation study/	49690
82	exp program evaluation/	17083
83	exp evidence based medicine/	995049
84	exp outcome assessment/	434786
85	exp randomized controlled trial/	507672
86	random* controlled trial.ti,ab.	100454
87	"clinical trial (topic)"/	94079
88	exp controlled clinical trial/	690327
89	multicenter study/	188788
90	random*.ti,ab.	1324555
91	(pretest or pre test).ti,ab.	22537
92	(posttest or post test).ti,ab.	23627
93	before after.ti,ab.	6772
94	qua?irandomi*.ti,ab.	115
95	nonrandomi*.ti,ab.	13067
96	exp open study/	32024
97	exp cohort analysis/	383288
98	exp longitudinal study/	115056
99	systematic review/	171907
100	"meta analysis (topic)"/	38039
101	81 or 82 or 83 or 84 or 85 or 86 or 87 or 88 or 89 or 90 or 91 or 92 or 93 or 94 or 95 or 96 or 97 or 98 or 99 or 100	2917168
102	"OST".tw.	2019
103	"opioid substitution".tw.	843
104	"methadone".tw.	17228
105	"MMT".tw.	3668
106	"methadone maintenance".tw.	4850
107	"buprenorphine".tw.	7895

#	Terms	Results
108	"Buprenorphine maintenance".tw.	343
109	"opioid replacement".tw.	160
110	"opioid agonist".tw.	3335
111	"opiate agonist".tw.	607
112	"opioid maintenance".tw.	528
113	"opiate maintenance".tw.	148
114	exp Buprenorphine/	15094
115	exp Methadone/	30629
116	exp Opiate Substitution Treatment/	1720
117	exp methadone treatment/	4247
118	exp buprenorphine plus naloxone/	1368
119	102 or 103 or 104 or 105 or 106 or 107 or 108 or 109 or 110 or 111 or 112 or 113 or 114 or 115 or 116 or 117 or 118	51124
120	80 or 119	602761
121	17 and 101 and 120	6803
122	limit 121 to (human and yr="2000 -Current")	6019

Searches conducted on 02/07/2018

Targeted searches were also conducted in Scopus and Google Scholar if no reviews or studies were identified by the review or individual study searches outlined above.

Table 3. Grades of evidence

Grade	Evidence
A	Consistent conclusions across meta-analyses, high quality systematic reviews of randomised controlled trials, or several randomised controlled trials
B	Evidence from one or two randomised controlled trials only
C	High-quality systematic reviews with some inconsistent conclusions from authors, or several consistent ecological studies or cohort studies
D	Cross-sectional association, case series suggesting outcome, or a single cohort study

Webappendix K: Description of evidence on the impact of interventions on other health outcomes

Table K1: Summary of the evidence of interventions to reduce harms associated with stimulant use

Intervention	Psychotic symptoms				Depression				Suicide/self-harm				Homicide				Overdose				Injecting risk behaviours			
	Effect	Size of effect	Level	Refs	Effect	Size of effect	Level	Refs	Effect	Size of effect	Level	Refs	Effect	Size of effect	Level	Refs	Effect	Size of effect	Level	Refs	Effect	Size of effect	Level	Refs
Individual/peer psychosocial interventions																								
Screening and brief intervention	×	Brief family - RR: 0.50 (0.10 – 2.43)	B[GEN]	149	-	-	-	-	↓	Screening – aIRR: 0.57 (0.41 – 0.78) Brief intervention – mean HR: 0.17 (0.07-0.46)	D[GEN] B[GEN]	150,151	-	-	-	-	↓	Opioid users, brief motivation interviewing - overdose risk behaviours IRR: 0.72 (0.59 – 0.87)	B*	152	-	-	-	-
Motivational enhancement therapy[#]	?	Mixed results when integrated with both CBT and family interventions for comorbid with SUDs	A[GEN]	153	?	May decrease symptoms when combined with CBT within alcohol use disorders (Hedge's g: 0.30 (0.11 – 0.47))	A[GEN]	154	×	No significant decrease in suicide attempt in youths	C*	155	-	-	-	-	-	-	-	-	↓	**SMD: -0.29 (-0.42- -0.15)**	**A***	156
Self-help interventions – written form, via phone, online	-	-	-	-	?	Mixed results about online self-help impact on depression symptoms compared to control	B[GEN]	157,158	?	Online self-help could decrease suicidal thoughts frequency but not severity compared to control	B[GEN]	157,158	-	-	-	-	-	-	-	-	-	-	-	-
Self-help interventions involving peers	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Cognitive behaviour therapy	×	RR 0.91 (0.63 – 1.32)	A[GEN]	159	↓	SMD -1.12 (-1.53 - -0.71)	A[GEN]	160	↓	Significant decrease in suicide attempts within substance users (5.3% vs. 35.3% TAU)	C*	155	-	-	-	-	-	-	-	-	↓	**SMD: -0.29 (-0.42-- 0.15)**	**A***	156
Family interventions	×	25-36 mths: RR 0.89 (0.72 – 1.10)	A[GEN]	161	?	Decreased depression symptoms compared to waitlist/treatment as usual, but not CBT	A[GEN]	162	×?	No significant difference in suicide attempts but potentially decrease suicide ideation with family interventions	C*	155	-	-	-	-	-	-	-	-	-	-	-	-
Multi-systemic therapy	-	-	-	-	-	-	-	-	↓	Multi-systemic therapy lowered youth 12 month suicide rates compared to hospitalisation	C*	155	-	-	-	-	-	-	-	-	-	-	-	-
Contingency management	-	-	-	-	↓	Decreased depression symptom between baseline (1.05±0.89) and 9-month follow (0.62±0.79)	C≠	163	-	-	-	-	-	-	-	-	-	-	-	-	↓	**SMD: -0.29 (-0.42-- 0.15)**	**A***	156
Community reinforcement approach	-	-	-	-	×	No significant difference by 24-month FU compared to coupons	B≠	164	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Acceptance and commitment therapy	-	-	-	-	↓	6-month FU compared to expressive writing – OR: 1.98 (1.02 – 3.83) (web-based)	B[GEN]	165	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-

Meditation-based therapies	-	-	-	-	↓	MD -4.51 (-7.47 - -1.55) (Mindfulness-based therapies)	B[GEN]	166	↓	Mindfulness on suicide rumination – Point estimate: -2.53 (-3.75 - -1.32)	D[GEN]	167	-	-	-	-	-	-	-	-	-	-	-	-
Pharmacotherapy and medication																								
Psychostimulants	-	-	-	-	✕	SMD: -0.07 (-0.48-0.34)	A	168	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Antipsychotics	↓	**SMD:-6.1 (-10.93—1.27)**	**A**	169	✕	SMD:-0.82 (-3.19-1.55)	A	169	?	Evidence is limited and inconsistent	C[GEN]	170	-	-	-	-	-	-	-	-	-	-	-	-
Dopamine agonists	-	-	-	-	✕	SMD 0.47 (-0.35-1.28)	A	171	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Antidepressants	-	-	-	-	↓	**MD -1.41 (-2.44–0.37)**	**A**	172	?	May have decreased risk of suicide among people continuing pharmacotherapy for depression	C[GEN]	173	-	-	-	-	-	-	-	-	-	-	-	-
Agonist pharmacotherapy	-	-	-	-					-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
HCV treatment	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
HIV treatment	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
STI treatment	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Public health and community-based interventions																								
Suicide prevention strategies	-	-	-	-	-	-	-	-	↓?	Depending on the prevention strategy, can either decrease suicides or mixed results (see **Table I3** for more details)	C[GEN]	173-175	-	-	-	-	-	-	-	-	-	-	-	-
Compulsory detention centres	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Therapeutic communities	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	↓	Opioid users: 0 vs. 31 overdose deaths	D*	176	-	-	-	-
Residential rehabilitation	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Other law enforcement interventions	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-

Notes on codes used in this table

Presence or absence of effect

✕ This intervention does not appear to have a significant effect upon the outcome
↑ This outcome may be increased by the intervention
↓ This outcome is decreased by the intervention
? Mixed or inconclusive evidence regarding the impact of this intervention on the outcome
- No evidence could be located of the impact of this intervention upon the outcome
also termed motivational interviewing.

Level of evidence

A Consistent conclusions across meta-analyses, high quality systematic reviews, or multiple randomised controlled trials
B Evidence from one or two randomised controlled trials only
C High quality systematic reviews with some inconsistent conclusions from authors; OR multiple consistent ecological studies, or cohort studies
D Cross-sectional association, case series suggesting outcome, single cohort study
@ Most studies examined couples-family interventions among clients receiving OST
*Evidence drawn from people who inject drugs and not specific to stimulant users, however we have no reason to believe this intervention would operate differently among stimulant users specifically.
≠ Evidence specifically for cocaine.
[GEN] Evidence drawn from people who do not have a substance use disorder

Table K2: Summary of the evidence of harm reduction and preventive interventions to reduce harms associated with stimulant use

Intervention	Psychotic symptoms				Depression				Suicide/self-harm				Homicide				Stimulant use			
	Effect	Size of effect	Level	Refs	Effect	Size of effect	Level	Refs	Effect	Size of effect	Level	Refs	Effect	Size of effect	Level	Refs	Effect	Size of effect	Level	Refs
Harm reduction and preventive interventions																				
Condom provision	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Provision of sterile injecting equipment	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Drug consumption rooms (DCRs)	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	?	DCRs starting to target smoking/sniffing so could lower public stimulant use	D	[177]
Use of safe inhalation methods																	✕	Reduced injecting but not overall use	C	[178]
HIV testing + informing of serostatus	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
HCV testing + informing of serostatus	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	✕	No impact	C*	[179]
PreP for HIV	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
PreP for STIs	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-

Notes on codes used in this table

Presence or absence of effect

✕ This intervention does not appear to have a significant effect upon the outcome
↑ This outcome may be increased by the intervention
↓ This outcome is decreased by the intervention
? Mixed or inconclusive evidence regarding the impact of this intervention on the outcome
- No evidence could be located of the impact of this intervention upon the outcome
also termed motivational interviewing.

Level of evidence

A Consistent conclusions across meta-analyses, high quality systematic reviews, or multiple randomised controlled trials
B Evidence from one or two randomised controlled trials only
C High quality systematic reviews with some inconsistent conclusions from authors; OR multiple consistent ecological studies, or cohort studies
D Cross-sectional association, case series suggesting outcome, single cohort study
@ Most studies examined couples-family interventions among clients receiving OST
*Evidence drawn from people who inject drugs and not specific to stimulant users, however we have no reason to believe this intervention would operate differently among stimulant users specifically.
≠ Evidence specifically for cocaine.
[GEN] Evidence drawn from people who do not have a substance use disorder

Table K3: Summary of suicide prevention strategies

Intervention	Effect	Size of effect	Level	Refs
Suicide prevention strategies				
Firearm restriction	?	Availability in home – OR: 3.24 (2.41 – 4.40) Introduction of laws: mixed results but	C*	[173]
Implication of barriers	↓	86% jumping reduction (79 - 91)	C*	[173]
Restricting barbiturates	↓	Restrictions occurred concomitantly with 55% decrease in suicide rate	C*	[173]
Reduced analgesic pack sizes		Estimated average reduction per quarter: 17 (-25 - -9)	C*	[173]
Contact or support post-suicide attempt	?	May be beneficial in low and middle- income countries	C*	[173]
School-based programmes	↓	OR: 0.45 (0.24 - 0.85)	C*	[173]
GPs programmes	↓	Decreased suicide rates in Western Europe countries	C*	[173]
Gatekeepers	?	Conducted in multilevel programs within institutionalised settings and aboriginal population lowered suicide rates	C*	[173,175]
Crisis hotlines/counselling	?	Limited evidence in United States with some callers helped but quality of calls varied	D*	[174]

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